

**MINDREADING DIFFICULTIES IN THE SIBLINGS OF PEOPLE  
WITH ASPERGER SYNDROME: EVIDENCE FOR A GENETIC  
INFLUENCE IN THE ABNORMAL DEVELOPMENT OF A  
SPECIFIC COGNITIVE DOMAIN**

**AND RESEARCH PORTFOLIO**

**PART ONE**

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**31<sup>st</sup> July 1999**

**Submitted in partial fulfilment of the degree of Doctor of Clinical  
Psychology within the Faculty of Medicine, University of Glasgow.**

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1. The first part of the paper is devoted to a discussion of the general principles of the theory of the structure of the atomic nucleus. It is shown that the structure of the nucleus is determined by the balance of the forces of attraction and repulsion between the nucleons. The forces of attraction are of two types: the strong interaction and the electromagnetic interaction. The strong interaction is responsible for the binding of the nucleons into a nucleus, while the electromagnetic interaction is responsible for the repulsion between the protons. The balance of these forces determines the stability of the nucleus.

2. The second part of the paper is devoted to a discussion of the experimental data on the structure of the atomic nucleus. It is shown that the experimental data are in good agreement with the theoretical predictions.

3. The third part of the paper is devoted to a discussion of the applications of the theory of the structure of the atomic nucleus. It is shown that the theory can be used to calculate the binding energy of the nucleus, the mass of the nucleus, and the probability of decay of the nucleus.

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# **1. Small Scale Service Evaluation Project**

**A study of epilepsy in people with learning disabilities  
receiving services from Community Learning Disabilities  
Teams.**

**Small-scale project submitted in partial fulfilment of the requirements for  
the degree of Doctor of Clinical Psychology**

**Prepared in accordance with the guidelines for contributors  
to the journal 'Seizure'.**

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## Abstract

People with epilepsy and learning disabilities pose a challenge in terms of clinical management and research investigation, and to date, the measurement of outcomes in this population has been limited (Espie, Kerr, Paul, O'Brien, Betts, et al, 1997). An audit within the Greater Glasgow Community and Mental Health Services was conducted during 1997 concerning adult epilepsy sufferers who have learning disabilities, and who are known to Community Learning Disabilities Teams (CLDTs) covering the Glasgow area. The present study provides a preliminary demographic analysis of these data. The primary purpose of the study was to identify patterns of service use of people with epilepsy and learning disabilities. It was anticipated that this would help to inform service planning and delivery. The study found that multiple seizure types were a common presentation, and rates of anti-epileptic drug (AED) polytherapy were high (49.8%), in a group of people who have learning disabilities and epilepsy. Rates of attendance at specialist services such as Neurology and Psychiatry were modest at 38% and 50% respectively. Given the multiple needs of this group who have been described as having *epilepsy plus*, services may not be offering these clients adequate management in terms of optimal treatment or assessment.

## Introduction

Epilepsy is the most common serious neurological condition affecting over 300,000 people in the UK (Wallace, Shorvan, & Hopkins, 1997). Within this group are specific sub-populations who co-present with additional conditions, learning disability being one such example. Epilepsy rates are highest of all in this subgroup, being between 21% and 50% and are positively correlated with degree of learning disability (Espie & Paul 1997). Despite the large numbers of affected individuals and their complex needs, epilepsy services have been shown in numerous studies to be deficient not only in the diagnosis and treatment of the condition, but also in the organisation of care e.g. poor follow up and discontinuity of care between GP's and hospital specialists (eg Taylor, Readman, Hague et al, 1994; Hopkins & Scrambler, 1997).

Diagnosis and treatment are further complicated in cases where there are no witnesses and the patient has little recollection of seizures, or where the patients' level of understanding or communication is limited, such as in people with learning disabilities (Paul 1997). The presence of additional neurological, psychological and social handicaps has long been associated with a more adverse prognosis (Rodin 1968; cited Espie & Paul 1997a). This has led to the term *epilepsy plus* being applied to those who present with these additional impairments, and whose diagnosis or treatment or management does not lead to adequate seizure control (Brown, Betts, Chadwick, Hall, Shorvan et al, 1993). People with learning disabilities may present with all of these additional problems. Other problems faced by those with a dual diagnosis include quality of life issues such as the

effects of perceived stigma, employment restrictions, risk of injury, and social restrictions such as being more dependent on carers. The occurrence of recurring, unpredictable seizures is undoubtedly a major factor affecting the life of a person with epilepsy. Seizure frequency, fear of seizures and self perception of epilepsy have all been shown to be predictors of well being in people with epilepsy (e.g. Leonard 1989; Kendrick 1997).

Monotherapy with one anti epileptic drug (AED) is the treatment of choice in epilepsy. Practise in learning disabilities however, shows that up to 40% of people receive polytherapy (Espie, Gillies, & Montgomery, 1990; Hogg, 1992). This tendency to overmedicate is due in part to the intractability of seizures in this population but is associated with increasing cognitive and behavioural side effects (Meador, 1994). There is evidence that reducing the number of AEDs prescribed can result in improved seizure control and in reductions in behavioural and social problems (e.g. Fischbacher, 1985).

People with epilepsy and learning disabilities pose a challenge in terms of clinical management and research investigation, and to date, the measurement of outcomes in this population has been limited (Espie et al, 1997c). An audit within the Greater Glasgow Community and Mental Health Services was conducted during 1997 concerning adult epilepsy sufferers who have learning disabilities, and who are known to Community Learning Disabilities Teams (CLDTs) which cover the Glasgow area. The present study provides a preliminary demographic analysis of these data. The primary purpose of the study was to identify patterns

of service use of people with epilepsy and learning disabilities. It was anticipated that this would help to inform service planning and delivery.

## **Method**

A questionnaire was designed comprising information on demographics; seizure frequency, type and pattern; medication; and contact with specialists available on request. There was also an open section inviting comments as to the nature of involvement of CLDT members with the person with epilepsy and /or their carers. The questionnaire was distributed amongst the four Community Learning Disabilities Teams which cover Glasgow, South East; South West; North East; and North West, to be completed by each individual's named worker within the team (i.e. the case manager). Data were also gathered from a short stay admission unit in the south of the city.

## **Results**

### **Demographic Information**

The audit included a total of 205 individuals all of whom had diagnosed epilepsy and learning disabilities, and were currently receiving a service

from one of the 4 CLDTs in Glasgow. The audit did not include 'inactive' cases on the CLDT register (i.e. those not currently receiving regular input from a CLDT health professional). Roughly equal numbers of responses were received from the four CLDTs [ NE= 48, NW=48, SW=57, SE= 43 , with 9 from a short stay NHS assessment unit]. There were similar numbers of males (n=100) and females (n=104). Age ranged from 16yrs to 65yrs and almost two-thirds of patients were under 36 years of age (see Table 1). The severity of learning disability was unstated in 106 (52%) cases, the proportions of people in each of the categories of mild, moderate, severe, and profound learning disability are also shown in Table 1.

***Insert Table 1 here***

## **Seizures**

The questionnaire adopted a simplified seizure typology (see Table 1). One-hundred-and-one individuals (49.3%) were reported as having tonic-clonic seizures. Forty-one (20%) also experienced absences, and 26 (13%) complex partial seizures. Overall, absences and partial seizures presented in around one-third of the sample and 9 (4.4%) were classified as having non-epileptic seizures. Seizure frequency is presented in Figure 1. Fifty-four people (26.3%) had seizures monthly, 27 of whom had single seizures and 8 had a cluster of seizures. A further 36 (18.5%)

had seizures weekly, 14 with single seizures and 7 a cluster. Twenty-two (10.7%) people had daily seizures, the pattern of which was evenly distributed between single, cluster and serial seizures. Twenty-three people (11.2%) had seizures once a year most of whom had a single seizure, and 25 (12.2%) had seizures of a less than yearly frequency.

***Insert Figure 1 here***

## **Pharmacological Treatment**

Eighty-four (41%) people were receiving anti-epileptic drug (AED) monotherapy, 42 (50%) taking Carbamazepine and 18 (21.4%) Sodium Valproate. Of remaining cases, 53 (26%) received 2 drugs [Common Drugs: Carb=29; Valproate=27; Phenytoin=9; Lamotrigine=5 ], 39 (19%) received three drugs [Common Drugs: Carb=21; Valproate=15; Lamotrigine=12 ], and 9 people were treated with 4 AEDs. Overall, 49.8% of the sample were being treated with AED Polytherapy.

The most commonly prescribed AEDs were carbamazepine which 107 (52%) people were prescribed, and sodium valproate 67 (32.7%). Phenytoin, lamotragine, and phenobarbitone were the next most

common AEDs, each prescribed in around 25-30 cases. Rectal diazepam was prescribed for 36 individuals (17.6%). The full range of AEDs prescribed and their relative use is presented in table 2.

***Insert Table 2 Here***

Figure 2 illustrates the relationship between seizure frequency and number of prescribed AEDs amongst the sample. It can be seen that people exhibiting poor seizure control (daily or weekly seizures) were more likely to be treated with AED polypharmacy in an approximate ratio of 3:1 (poly:monotherapy). Those experiencing monthly seizures were represented equally (1:1) whereas those with 1 seizure per year or less were much more likely to be on AED monotherapy (1:2.5).

***Insert Figure 2 here***

## **Roles of CLDT Staff**

Thirty-six (21%) of CLDT members regarded their input as 'primary' in managing an individual's epilepsy, with 95 (56%) classifying their input as 'secondary'. A further 26 (15%) stated they had no input into their clients' epilepsy, and the remaining 14 (8%) did not complete this section. When asked to comment on the nature of their involvement with clients the majority of CLDT staff reported that offering support and advice to carers along with monitoring seizure frequency were their principal roles. Figure 3 presents an overview of perceived roles.

***Insert Figure 3 here***



## Discussion

It was noticeable that none of the clients considered in this study were over the age of 65 years. This contrasts with a study by Muir, Bradley, Wood, Murray, & Brodie, (1996) who conducted an audit of patients receiving AED therapy in 25 general practises in Glasgow, and found that 19% of their sample were over 65yrs. There were also differences found in the frequencies of some forms of seizure between the current sample and one studied by Tobias, Brodie, & Brodie, (1993). The latter study examined 1000 consecutive referrals to an epilepsy clinic at the Western Infirmary and found rates of absence seizures of 4% compared with 21% in the current study, myoclonic seizures in 3% compared with 6.5% in the current study, and rates of non-epileptic seizures in 1% compared with 5% in the current study.

The higher frequency of these seizure types is a consistent finding in studies of people with epilepsy and learning disabilities, reflecting a more invasive neuropathology. Absence type seizures are often thought to be less serious than other seizure types. However, recurring gaps in awareness may severely impair the quality of attention available to an individual leading to deficits in learning potential and learning outcome (e.g. Espie & Paul 1997a). These authors also point out that preoccupation with seizure frequency as an outcome measure in both research, and in clinical practise, has led to a lack of recognition of the importance of inter-ictal well-being (Espie & Paul, 1997a). The high rate

of Absence events present in the individuals in this study would appear to provide testimony to this need for more consideration into enhancing the quality of cognition between seizure events.

Recording of seizure activity has traditionally focused on seizure frequency, often at the expense of accurate classification of seizure form. Clinical practise relies heavily on the patients self report. Even during EEG assessment, seizures are rarely observed by clinicians. Patients with learning disabilities are less able to clearly communicate the nature of their experiences and so accurate diagnosis requires careful coding and classification of observable behaviour. There is also a need to assess the impact of a persons epilepsy on their quality of life from their own perspective, which has led to the development of new scales such as the "Epilepsy Outcome Scale" (Espie, Paul, Graham, Sterrick, Foley et al, 1997b). The EOS scale measures client concerns on a number of dimensions including, "Concerns about: seizures; drugs; injury; daily life".

The rates of monotherapy in this study was relatively low at 45% (n=72). This compares with a rate of 76% in the GP sample studied by Muir, Bradley, Wood, Murray, & Brodie (1996), and a rate of 58% in the sample of Neurology patients studied by Tobias, Brodie, & Brodie (1993). The rates of polytherapy were higher at 47% (n=80), than in some other studies looking at clients with epilepsy and learning disabilities e.g. 40% found by Espie et al (1990). However, there were a large number of people prescribed two AEDs (31%). When considering combining AEDs,

clinicians must also consider neurotoxic effects. Newer AEDs such as Lamotrigine, Gabapentin, and Ethosuximide may offer a greater range of combination therapies, and there is currently, great interest in delineating which are the most effective treatments for which form of epilepsy, both as monotherapy and as rational polytherapy. As an example, Paediatricians have been interested in the use of lamotrigine because it is effective in children with idiopathic generalised seizures and does not impair cognition (e.g. Dichter & Brodie, 1996). However, there has been concern about the higher costs associated with the newer AEDs as they have not been widely demonstrated to be more clinically effective than the older AEDs such as Carbamazepine or Valproate, and can also be associated with toxic side effects (Dichter & Brodie, 1996).

There has been debate around how Epilepsy services should be organised and co-ordinated e.g. Muir et al (1996), who as part of the West of Scotland Epilepsy Research Group (WOSERG) suggest a 'shared care model' co-ordinated by the GP. The views of the professionals working within CLDTs in this study suggest that they largely see their input as being a secondary one. The majority of respondents emphasising activities such as monitoring seizures, offering support, advice and education to clients & carers, and liaising with other professionals as key aspects of their input into clients epilepsy. Activities such as Behaviour management, general and mental health concerns, and monitoring bloods were mentioned less often and could be areas where CLDTs could take a more major role. For example, the functional

analysis of behaviour can contribute towards a greater understanding of whether a problem behaviour is seizure related and possibly less likely to be under an individual's control, or whether it is related to the sequelae of having a diagnosis of epilepsy.

## **Conclusion**

The present study has found low rates of monotherapy in a group of people who have learning disabilities and epilepsy. Rates of attendance at specialist services such as Neurology and Psychiatry were modest at 38% and 50% respectively. Given the multiple needs of this group who have been described as having *epilepsy plus*, services may not be offering these clients adequate management in terms of optimal treatment or assessment. Greater attention and research into areas such as quality of life, and the functional analysis of problem behaviour may provide useful interventions, which may become part of the service offered by CLDTs.

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**Table 1. Summary data showing age range (n=194), severity of learning disability (n=99), and Seizure type.**

Age Range	% of cases	Severity of Learning Disability	% of cases	Type of Seizure	% of cases	n
16-25 yrs	26.8	Mild	7.8	Tonic-Clonic	49.3	101
26-35 yrs	33.2	Moderate	15	Partial	13	26
36-46 yrs	20	Severe	11	Absence	20	41
47-65 yrs	14.6	Profound	14	Unclassified	10.2	21
		Borderline	1	Non-Epileptic	4.4	9
		Unstated	57	Myoclonic	5.9	12



Figure Legend

Figure 1. Seizure Frequencies in individuals including all degrees of learning disability and seizure type (n=165).

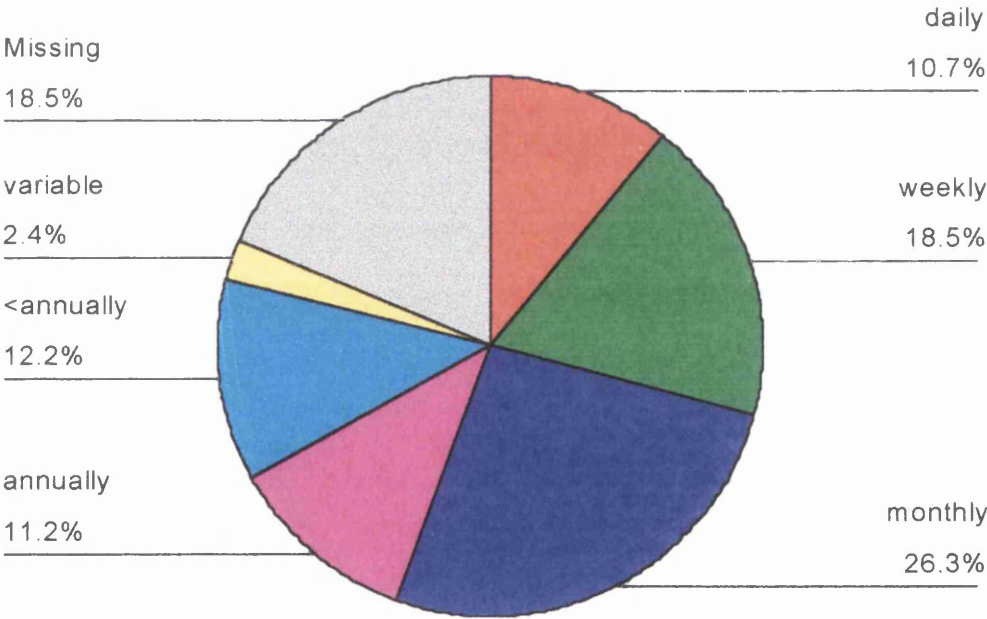
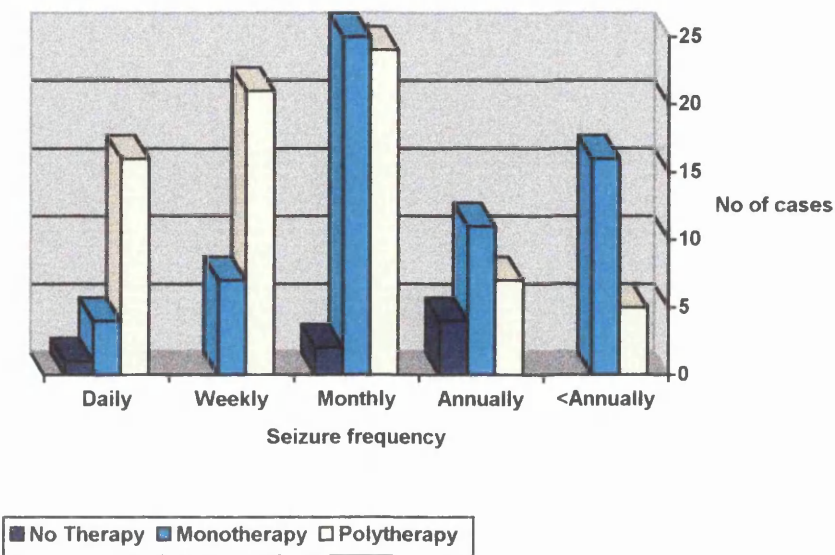


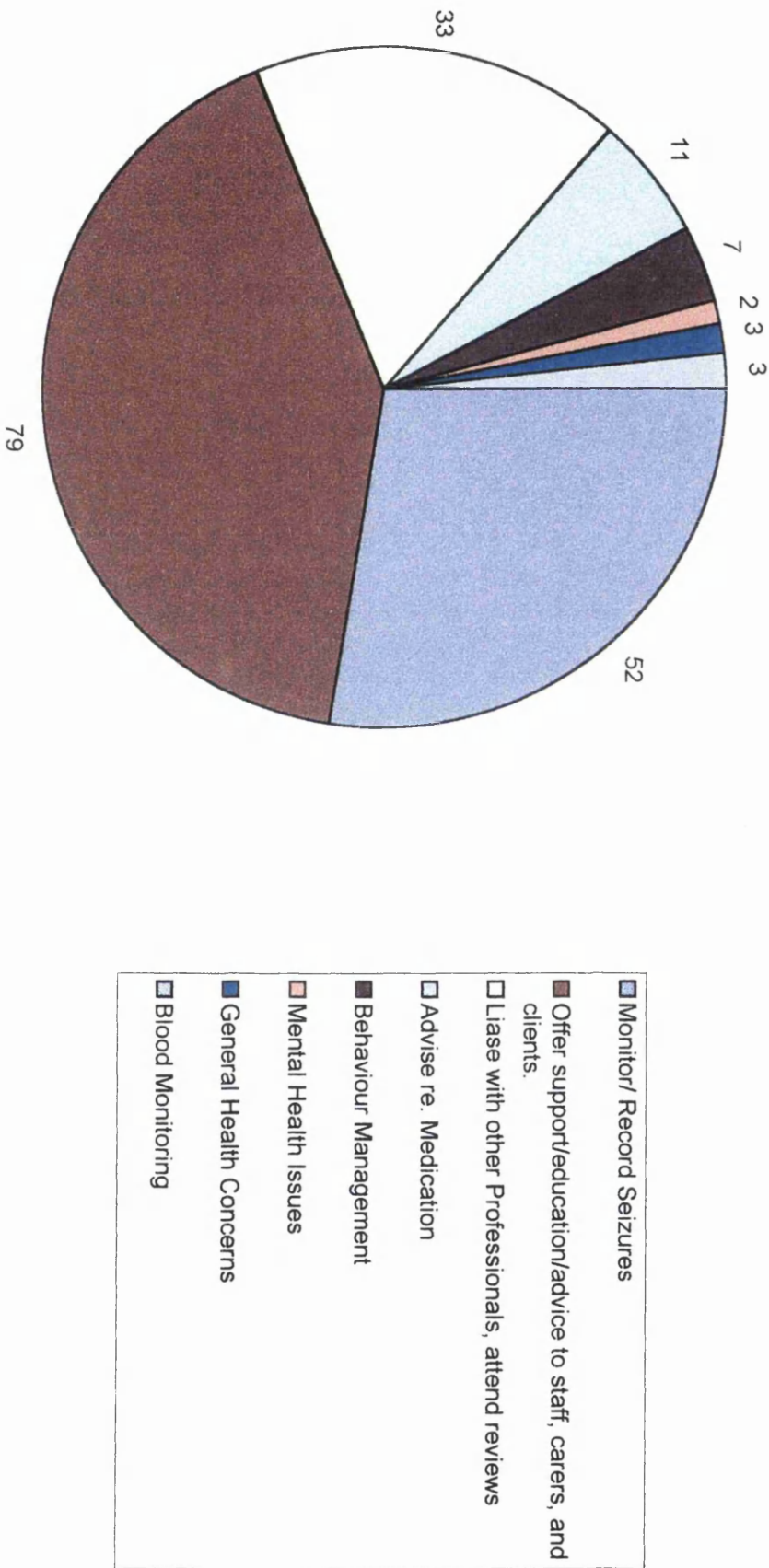
Figure 2. Relationship between drug use and seizure frequency.



**Table 2. Reported use of anti-epileptic drugs in rank order of use (sample=205).**

<b>Medication</b>	<b>No of Prescriptions</b>	<b>% Total Cases</b>
Carbamazepine	107	52
Sodium Valproate	67	32.7
Lamotrigine	29	14
Phenytoin	27	13.2
Phenobarbitone	24	11.7
Vigabatrin	11	5.4
Gabapentin	9	4.4
Primidone	8	3.9
Clonazepam	6	2.9
Clobazam	4	2
Topiram	3	1.5
Ethosuximide	0	0
<i>Oral Diazepam</i>	17	8.3
<i>Rectal Diazepam</i>	36	17.6

**Figure 3. Frequency of statements made by CLDT members when asked about their input with clients' epilepsy**



## **2. Major Research Project Literature Review**

**Mindreading: A review of the literature on 'theory of mind' abilities in individuals with Autism, Asperger Syndrome, non-Autistic clinical groups, and normally developing children.**

**Prepared in accordance with the notes for contributors to the  
'Journal of Child Psychology and Psychiatry'.**

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## **Abstract**

'Theory of mind', the ability to make inferences about other's mental states, appears to be a cognitive capacity that underlies human's ability to engage in complex social interaction. The 'theory of mind' deficit account of autism suggests that the communication, socialisation and imagination handicaps of autistic individuals spring from their inability to represent and attribute mental states, such as intentions, beliefs, and desires. Strong claims have been made over the past decade for the significance of this ability, or rather disability, in the social/cognitive profiles of autistic children. Indeed, it is claimed that it is this "mind blindness" that is the core of the disorder. Recent studies have suggested that these 'theory of mind' deficits can be expressed by first-degree relatives of children with Asperger Syndrome (a mild form of Autism), albeit at a lesser severity of deficit. The nature and extent of these deficits in children and adults with AS/Autism are reviewed, as is the progression of these abilities in normally developing children. The article concludes by describing a planned study which aims to provide evidence that these 'theory of mind' deficits may exist in a lesser form, in the siblings of children with Asperger Syndrome.

## **The Autistic Spectrum Disorders**

Autism and Asperger syndrome are pervasive disorders of development characterised by abnormal difficulties in social relationships, communication, and imagination. Current Psychiatric classification systems (e.g. DSM IV, American Psychiatric Association, 1994; ICD-10, World Health Organisation, 1993) have attempted to provide a way to differentially diagnose children with Pervasive Developmental Disorders (PDD) into sub-categories of Autism, Asperger syndrome, and Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS). Within this broad class of disorders, affected individuals share social and communicative impairments and restricted, repetitive patterns of interests and behaviours (Wing, 1981). These classification systems suggest that a diagnosis of Asperger Syndrome (AS) applies when there is no clinically significant delay in language development, and intelligence is in the normal range (Prior, Eisenmajer, Leekam, Wing, Gould et al, 1998).

There is debate as to whether the autistic disorders represent a continuum or whether they are separate disorders. Since autism was first described by Kanner (1943) researchers have been speculating about the role of genetic factors in the aetiology of autism. Folstein & Rutter (1977) suggested a genetic hypothesis, conceptualising a continuum of underlying genetic risk for autism, with the full syndrome as the most severe phenotype. These authors suggest that it is not autism as such that is inherited, but rather a pervasive cognitive

deficit of which autism is one part. Twin studies offer strong support for the genetic contribution to autism by indicating a greater MZ than DZ concordance for autism and autistic spectrum disorders (Folstein & Rutter, 1977; LeCouter, Bailey, Rutter, & Gottesman, 1989). For example, Bailey, LeCouter, Gottesman, Bolton, Simonoff et al, (1995) combined their data with that from earlier studies and found an MZ concordance rate of 60%, and a DZ rate of 0%.

There is also heterogeneity of the clinical presentation of autistic disorders (Rapin, 1994); a wide range of cognitive abilities (Klin & Shephard, 1994); a diversity of neurochemical findings both peripherally (Anderson, Freedman, Cohen, Volkmar, Hoder et al, 1987), and centrally (Narayan, Srinath, Anderson, & Meundi, 1993); and a multiplicity of aetiologies of the autistic syndrome (Rubenstein, Lotspeich, & Ciaranello, 1990). This lack of a unifying central hypothesis regarding ultimate causation, combined with the heterogeneous behavioural presentation in the autistic disorders, has led some to suggest that there may exist a spectrum of autistic disorders (e.g. Wing 1989). Differential epidemiological estimates of Asperger syndrome and autism have been published (Ehler & Gilberg, 1993). However, attempts to differentiate these subgroups objectively have not yet led to any consensus.

Autism as a syndrome – the autistic spectrum of disorders – includes many different sorts of children who may have many different sorts of brain dysfunction that have in common particular behavioural, social and communicative impairments. That they share this dysfunction in a common brain system(s), with or without dysfunction in other systems, is a widely held,



unproven assumption (Rapin 1987; Waterhouse 1994). Delineating specific behavioural or cognitive phenotypes has the potential to isolate more specific subgroups within the autistic spectrum. In the case of autism it is suggested there is a basic dysfunction in those systems serving mentalising functions i.e. attributing mental states such as beliefs, desires, and intentions as being causal in explaining and predicting the behaviour of other's (Baron-Cohen, 1989; Frith, 1989). This impairment includes deficits in understanding that seeing leads to knowing (Baron-Cohen & Goodhart, 1994), distinguishing mental from physical entities, and making appropriate distinctions between appearance and reality (Baron-Cohen, 1989a).

Further developmental evidence for this 'folk psychology' appears to be present from at least 12 months of age (Baron-Cohen, 1994; Gergely, Nadasdy, Gergely & Biro, 1995; Premack, 1990; Rochat, Morgan & Carpenter, 1997). These studies have shown that infants show dishabituation to the actions of 'agents' that appear to violate goal-directedness; expect agents to express emotions, and this to be consistent across modalities (for example, between face and voice); and are highly sensitive to where another person is looking, and will strive to establish joint attention.

## **Mentalising & 'Theory of Mind' (ToM)**

A range of cognitive deficits has been found in autism (Ozonoff, Pennington, and Rogers, 1991), and has led to the hypothesis that cognitive deficits may underlie the social impairment. One aspect of social cognition which has been shown to be impaired in autism is the ability to fully develop a 'theory of mind', which entails being able to postulate the existence of mental states and then using them to explain and predict another person's behaviour (Baron-Cohen 1989). The 'theory of mind' deficit account of autism suggests that the communication, socialisation and imagination handicaps of autistic individuals spring from their inability to represent and attribute mental states (Frith, 1989; Leslie, 1987, 1988). Strong claims have been made over the past decade for the significance of this ability, or rather disability, in the social/cognitive profiles of autistic children. Indeed it is claimed that it is this "mind blindness" that is the core of the disorder (See Baron-Cohen, 1989; Frith, 1989; Happe, 1994).

Baron-Cohen, Leslie, & Frith (1985) used the "Sally-AnneTest"- a puppet play during which an object is moved whilst a character is absent, to examine 'theory of mind' abilities in three groups of children (see Appendix 2.0 for example of this test). They found that whilst normal children of 3-4 years, and children with Down Syndrome of below average intelligence, could attribute a false (and therefore different) belief to a character i.e. predicting where the character would search for the object, 80% of autistic children of normal intelligence showed no evidence of this ability. To pass this test, the subject must attribute a belief to another person. This ability can be termed "first order belief attribution" (Wimmer

& Perner, 1983). Normal 6-7 year old children are able to make “second order belief attributions” or, the ability to think about another person’s thoughts about a third person’s thoughts about an objective event. Baron-Cohen (1989) found that autistic subjects who were able to pass first order ToM tasks were severely impaired relative to a group of younger normal children (who had lower verbal IQ’s), on a second order ToM task involving answering questions about a characters beliefs about another character during a puppet play.

Prior et al (1998) used a cluster analytic technique to elucidate the discriminating features between individuals with high functioning autism (HFA) i.e. IQ approximately within the normal range, and Aspergers syndrome (AS). They assessed participants (N=135) using detailed behavioural checklists (Autistic Spectrum Disorders Checklist; Rapin, 1996), and also first and second order ‘Theory of Mind’ tasks, which require reasoning about behaviour in terms of underlying mental states. The theory of mind tasks used were the “Sally-Anne” task (Baron-Cohen et al, 1985; Wimmer & Perner, 1983); and the “Box of Smarties” task (Perner, Leekam & Wimmer, 1987), both first order tests.

The study by Prior et al was notable for it’s large sample size and the higher age and level of functioning of the subjects, compared with previous cluster analytic attempts. Participants congregated into three clusters which roughly corresponded to the clinically familiar groups of HFA, AS, or PDD-NOS, differing on theory of mind performance and on verbal abilities. One of the clusters (B) included 58% of those diagnosed as having Aspergers syndrome, and became

the putative Aspergers cluster. The children within this cluster were less socially impaired, and more desiring of social interaction with their peers. They were more likely to have pedantic-style, egocentric conversations, usually focused on their own current preoccupation's or special interests, whilst their performance on 'theory of mind' tasks was superior to those in the putative HFA cluster (A). Almost all of those in the 'Aspergers' cluster were able to pass first order ToM tasks, and over half were able to pass second order tasks. The putative HFA cluster (A) was described as more impaired in terms of social, and cognitive impairments, and were more impaired on ToM tasks although quantifying this difference was hampered by poor compliance to the task demands in the HFA cluster. The authors suggest their results support a spectrum concept for the autistic disorders, with the B and C clusters towards the upper end of the spectrum in terms of behavioural, cognitive, and communicative functioning. They further suggest that mentalising deficits may be primarily associated with developmental cognitive and language delay rather than simply autistic disorders.

### **Specific Developmental Delay or Developmental Deviance**

Developmental delay implies a pattern of development that conforms to typical developmental processes but simply progresses at a slower rate, whereas deviant development refers to patterns which cannot be understood within that

framework. The theoretical framework for theory of mind implies a degree of synergy between social interaction and theory of mind development. For example, Perner, Ruffman, and Leekam (1994) found that the theory of mind (first-order ToM task) performance of normal 3-4 year olds was positively related to the size of family (number of siblings) from which they came. Given that theory of mind abilities normally emerge during the pre-school years, social experience relevant to theory of mind development must derive largely from day to day interactions with family, especially parents and siblings, and friends. However, it is unclear whether the 'social experience' theory has a causal role in the development of theory of mind abilities in autistic children. It has been debated whether the deficits in theory of mind abilities in autistic children represent a specific developmental delay in the normal sequence, or whether they represent developmental deviance, or both (Burack, 1992; Baron-Cohen, 1992). Baron-Cohen (1989) found that autistic subjects passing first-order ToM tests may be chronologically very delayed in the development of these abilities—on average by seven years in contrast to normal subjects, and delayed relative to their MA as well.

There is evidence that some autistic children can pass both first and second order ToM tasks after periods of (often considerable) delay, and that those who pass one theory of mind task (of a given level) tend to pass all theory of mind tasks (of an equivalent level) they are set (Baron-Cohen, 1989b; Happe, 1991). However, given the enduring and pervasive nature of many of the deficits shown by autistic individuals, it is difficult to conceptualise their abilities in social communication within a framework of typical development. Holroyd & Baron-

Cohen (1993) assessed the development of theory of mind abilities using the Sally-Anne task in 17 autistic subjects, and re-assessed them eight-years later (mean age at first testing= 12 yrs; second testing 19.8 yrs). There was no statistical change in the group across the time-span, prompting the authors to conclude that for the majority of those people with autism, there may be little development of a theory of mind beyond that reached in childhood. This is often confirmed by clinical experience, although developing alternative 'compensatory' strategies are often a focus for intervention in improving social performance.

Burack & Volkmar (1992) examined developmental progression in receptive and expressive communication domains in both high and low autistic children and non-autistic learning disabled children of similar IQ. They found that all four groups showed a similar-sequence of development as normal children.

However, developmental regressions, particularly in communication realms, were often found in autistic subjects, which often represented permanent losses of capabilities and were indicative of poor prognosis. The findings of developmental 'unevenness' in autistic children suggests at least some deviance in developmental sequencing, although the factors moderating developmental progression are unclear. Longitudinal research looking at specific cognitive abnormalities may provide greater insight into the question of deviance versus delay. Yirmiya, Erel, Shaked, & Solomonica-Levi (1998) in a meta-analysis of the literature, concluded that deficits in theory of mind are not unique to autistic spectrum disorders, as they are also manifested by learning disabled individuals. However, what may be unique to autistic conditions is the severity of the impairment.

### **ToM deficits in non-autistic clinical groups**

Russell, Hosie, Gray, Scott, Hunter, et al (1998), examined theory of mind abilities in Deaf children aged between 4-16 years (N=32) using a false belief task similar to the “sally-Anne” task (Baron-Cohen, 1985). They found that increasing ability was positively associated with increasing chronological age. The percentages of children passing were 17%, 10%, and 60% for the youngest, middle, and oldest groups, respectively. Their data suggested that it is only after the age of 13 years that a majority of deaf children can be expected to pass a ToM test of the sort passed by normally developing children at around the ages of 4-6 years.

Minter, Hobson, & Bishop (1998) compared theory of mind deficits in congenitally blind children to sighted children matched for verbal IQ. The visually impaired children’s performance on two theory of mind tasks was significantly poorer than that of their sighted peers (only 9/20 visually impaired subjects passing a False belief question, compared with 18/20 of the normally sighted children matched for chronological age and Verbal mental age). However, most of the visually impaired children could make some adjustment to another person’s false beliefs. The tasks used were the “teapot task”, and the “Boxes” task - ‘tactile’ versions of the original Wimmer & Perner false belief task (see above). A number of children with severe visual impairment experienced difficulties in judging what another person might believe on the basis of touch, when this belief no longer corresponded with the children’s knowledge of

present reality. This is interesting as many theorists have emphasised how joint visual attention between a young child and others may constitute an important precursor to 'theory of mind' understanding e.g. Baron-Cohen (1989; 1995); Baron-Cohen et al (1996). Minter et al provide some evidence for a specific impairment in ToM in children deprived of one important source of understanding about the nature of mental states, that of shared visual experience.

Happe (1995) in an overview of earlier ToM studies concluded that, whereas the majority of normally developing children passed 1st order ToM tests by the time they had a verbal mental age (VMA) of 4 years, the VMA of autistic children who did so was about 9 years 7 months. All of the above studies suggest a developmental delay/deviance has affected the performance of these variously disabled groups on ToM tasks, in either a specific way e.g. in studies of deaf or blind children, or else in a more pervasive and enduring way e.g. in the studies using autistic children.

### **Mentalising and Verbal Abilities**

A major issue within the theory of mind literature concerns the relationship between language and mental state awareness, which is very complex. It has now become clear that there are discernible relationships between verbal cognitive abilities and the capacity to demonstrate theory of mind capabilities



(e.g. Ozonoff, Rogers, & Pennington, 1991). Baron-Cohen (1989) found that whilst autistic children who were able to pass first-order ToM tasks tended to have a higher high verbal MA than those who failed, there were subjects with similarly high verbal MA's who failed the tests. Therefore, high verbal MA is a necessary but not sufficient condition for the development of a theory of mind in autistic children, even at the simplest level of first order belief attribution. In contrast the social cognitive abilities of normal children seemed to be independent of verbal MA beyond an MA of 4 years.

Happé (1994) found that although many high functioning autistic subjects in her study did use verbally expressed mental state concepts (e.g. "think") to explain the behaviour of story characters they did not use them appropriately. Happé also found that those autistic subjects who failed first-order ToM tasks ('Sally-Anne'; 'Smarties') had significantly lower VIQ's than those who passed. The author then argues that verbal IQ (as a measure of communication competence) and theory of mind abilities are not independent measures since VIQ is involved in the variable of interest i.e. theory of mind ability. Several studies have shown good performance on theory of mind tasks in learning disabled samples despite very low verbal IQ (see Yirmiya, Erel, Shaked, & Salamonica-Levi, 1998).

It would appear from the evidence to date that the role of verbal IQ in influencing theory of mind abilities has a different significance in autistic children, as compared to normal, and to learning disabled children. Because of the difficulty in creating 'pure' tasks that rely on a single cognitive ability it has traditionally

been difficult to determine which aspects of task performance are due to linguistic ability, or to 'pure' theory of mind ability. A problem inherent in many of the procedures used in the above studies concerns the use of conversationally based answers to ToM tests. For example, Siegal & Peterson (1994) analysed the conversational dynamics of false belief tasks, and found that varying the question used in a classic first-order task from, "Where will Maxi look to get the chocolate?" to "Where will Maxi look first of all?" resulted in normally developing children becoming significantly more likely to judge correctly that 'Maxi' will search in the last place he saw the chocolate. Therefore, the issue of validity may be compromised by using dependant measures that are conversationally based.

### **Neuro-biology and Theory of Mind**

Some theorists regard the emergence of theory of mind as being dependant upon the biological maturation of genetically based neurocognitive substrates, such as those underlying *metarepresentation* and *shared attention* (Baron-Cohen & Swettenham, 1996; Leslie, 1987, 1994). Baron-Cohen, Ring, Moriarty, Schmitz, & Costa, (1994) using SPECT scans of the frontal lobes in a group of 'normals', investigated whether recognition of mental state terms contained within a word-list, might be localised in the 'normal' brain. An autistic group had already been found to be impaired on the task relative to the normal group during an earlier phase of the study. The SPECT results implicated the orbito-

frontal cortex as the basis of this ability. The evidence for the orbito-frontal hypothesis of theory of mind is discussed more extensively by Baron-Cohen & Ring, (1994). Interestingly, patients with orbito-frontal lesions show loss of interest in social contact, and impaired social judgement (Eslinger & Damasio, 1985; Price, Daffner, Stowe et al., 1990).

There is also a growing literature concerned with the links between 'executive functioning' and theory of mind performance e.g. Hughes (1998). The term 'executive function' is used to encompass the processes (e.g. planning, inhibitory control, attentional flexibility, working memory) that underlie flexible goal directed behaviour (Duncan, 1986). Hughes found in particular, that children's deceptive abilities (thought to represent an important aspect of ToM) were closely related to success on tests of inhibitory control. Hughes, Plumet, & Leboyer (1999) found that poor executive control on the ID/ED Test and the Tower of Hanoi was a characteristic of a subset of siblings of autistic children. However, the small number of siblings failing both tasks (n=6) compared to the number failing from the 'normals' group (n=2) were too small for statistical analysis and so cannot be taken as evidence that siblings were more likely than controls to show pervasive problems of executive function. Hughes et al also suggest that executive dysfunction may give rise to everyday behavioural problems such as, repetitive behaviour, circumscribed interests, difficulties coping with novel situations, and distractibility, whereas separate impairments cause the deficits in sociability and communication that are the hallmark of autism (e.g. Baron-Cohen, 1995).

It is possible of course that children's theory of mind is best conceived as multifaceted. If so, separate aspects of ToM may be linked to different component processes e.g. executive functioning skills, and other higher order cognitive processes such as metarepresentation, as well as basic perceptual processes such as hearing and sight. As a result, age related improvements on theory of mind tasks may owe more to children's growing strategic abilities than to their developing true understanding of mind (see Russell, Jarrold, & Potel, 1994; also McGregor, Whiten, & Blackburn, 1998).

Ozonoff, Rogers, & Pennington (1991) found that a minority of high functioning Autistic children were able to pass both first and second-order 'theory of mind' tasks. However, Baron-Cohen & Jolliffe (1997) argued that the lack of deficits in these studies was due to the tests being too simple, being simply probes for a 4yr old (i.e. first-order theory of mind tasks) and 6yr old (i.e. simple second order theory of mind tasks) level of mindreading ability. Studies in the past have suggested that around 20% of high functioning adults with Autism can pass *second order theory of mind* tasks, usually passed by normal children around the age of 6 years. However, when subjects are tested at a nine-year-old level, deficits are again revealed (O'Riordan, Baron-Cohen, Jones, Stone, & Plaisted, 1996).

Bowler (1992) found that of a group of children with AS (n=15), 93% and 73% were able to pass first and second-order ToM tasks respectively. This compared with 93% and 80% of an age matched control group of normals, and 73% and

67% of a group of schizophrenic subjects matched for IQ. The most notable finding was the performance of the AS group on the 2<sup>nd</sup> order ToM task, which was much greater than that shown by the group of 'able' autistic children used by Baron-Cohen (1989a), none of whom could solve such a task. However, the mean chronological age of the Baron-Cohen group was 15.3 years versus 26.7 years in the Bowler group. The findings of the studies by Bowler, and Ozonoff et al (1991) suggest that subjects with high-functioning autism can be discriminated from those with AS on their ability to solve theory of mind tasks and on measures of verbal memory. This raises the question of whether they are separate disorders or different manifestations of an underlying common pathology.

The notion of an autistic 'continuum' as developed by Wing and Gould (1981) implies that people with AS and classic autism represent sub-sets of a larger population of people with social impairment, with AS individuals showing less global intellectual impairment and less impaired language skills.

Further to the 'continuum' account, Baron-Cohen & Hammer (1997a) report a series of experiments looking at normal sex differences on tasks of social cognition and spatial abilities, and also at children with AS/Autism and a group of parent's of children with AS. These experiments are reported below, the reported differences were statistically significant.

1. normal males (mean speed=46.2secs, sd=20.5) were superior to normal females (mean speed=66.7, sd=36.7) on the *Embedded Figures Test (EFT)*.
2. Normal females (mean score=21.8, sd=1.8) were superior to normal males (mean score=18.8, sd=2.5) on the *Eyes Test* (see below for description of this test).
3. Nine year old girls were superior to nine year old boys on the '*Faux Pas*' Test (identifying which of three characters "said something they shouldn't have" in a story), girls mean score=7.3 (sd=2); boys mean score= 4.9 (sd=2.7).
4. Adults with AS/HFA were superior to age matched normals on the *EFT*, mean speed in seconds= 29.28 (sd=21.6) for the HFA subjects, versus mean speed=32.2 (sd=27) in the AS group; versus mean speed=52.6 (sd=32.6) in the controls. The difference between AS/HFA versus normals was statistically significant;
5. Adults with AS/HFA were impaired relative to age-IQ matched normal controls on the *Eyes Test*, mean score=16.3 (sd=2.9), versus control mean score of 20.3, (sd=2.63).
6. Children with AS/Autism were impaired on the '*Faux Pas*' test relative to normal age-mental age matched controls, the AS/Autism children had a mean MA of 13 years but their mean score was equivalent to that of normal 7 to 8 year olds.

7. Mother's of children with AS were significantly faster than 'normal' mothers on the *EFT* mean=48.6, (sd=31.8); versus mean=66.7, (sd=36.7), as were AS fathers, mean score= 32.8 (sd=17.7), versus male controls mean score=46.2, (sd=20.5).
8. Parent's of AS children were impaired on the *Eyes Test* relative to normal controls, AS mothers mean score=18.9, (sd=2.1) versus control mean score=22.1, (sd=2); and AS fathers mean score=17.3, (sd=1.6) versus control mean=19.5, (sd=2.6).

They conclude from these experiments that outcomes reflect the existence of sex-linked neurodevelopmental processes in the population, and that autism is an extreme form of the male neurodevelopmental pattern. Hans Asperger himself (1944) said, "the autistic personality is an extreme variant of male intelligence". The mechanism/s through which the AS/Autism phenotype might appear are unclear, but might include having two parents, both of whom have the brain type associated more with male sex. Therefore, the continuum model implies that the existence of an AS brain type would predict greater degrees of this phenotype (in a lesser form) in first degree relatives.

In order to advance the hypothesis that theory of mind deficits were an enduring trait in autistic spectrum disorders, Baron-Cohen, Jolliffe, Mortimore, & Robertson (1997b) developed an '*adult*' theory of mind test, the "Eyes Test". This test was suggested to offer a greater level of difficulty and discrimination than the earlier belief attribution tasks. The test involves inferring the mental state of a person just from the information contained in photographs of persons'

eyes. They found that a group (n=16) of adults with high-functioning Autism (n=4) or AS (n=12) (mean age 28yrs; mean IQ 105) showed mind-reading deficits relative to age matched normals (n=50), and a clinical control group who all had Tourette Syndrome (n=10). The Autism/AS group mean score was 16.3 from a possible 25 (sd=2.9), the normals group mean was 20.3 (sd=2.6), whilst the Tourette Syndrome group mean score was 20.4 (sd=2.6). The differences between the Autism/AS group and the other groups were statistically significant ( $p = 0.0001$ ). However, given the well-documented difficulties in social relationships experienced by many Tourette's children (see Bawden, Stokes, Camfield, Camfield, & Salisbury, 1998), this may not have been the ideal control group.

As mentioned above, Baron-Cohen & Hammer (1997c) again used the "Eyes Test" to examine ToM deficits in the *parents* of Asperger Syndrome children. They hypothesised that the relatives of people with Aspergers' or Autism may not have the condition itself but may have a *lesser variant of the disorder*. They found qualitatively similar impairments in parents of AS children (n=30), relative to parents of non-affected children (n=30), but at a lesser severity of deficit. The difference between group scores was small but statistically significant, AS father's group mean= 17.3 (sd=1.6), compared to control males group mean of 19.5 (sd=2.6), ( $p < 0.004$ ). AS mother's group mean= 18.9 (sd=2.1) compared with control females group mean of 22.1 (sd=2.0), ( $p < 0.0001$ ). This raises the possibility that a lesser variant of one of the 'core' impairments in AS and Autism may be inherited and subtly expressed by relatives who are not autistic.



In line with this finding, several studies of families with a child who has AS have found an increased rate of AS profiles amongst other relatives. These profiles included increased incidence of communication disorders, specific learning disabilities, ADHD, and varying degrees of cognitive disabilities (August, Stewart, & Tsai, 1981; Gilberg, 1991). As well as various deficit profiles there have also been studies suggesting relative strengths in autistic children. Examples include visuo-spatial tasks such as Block Design of the WISC-R (Shah & Frith, 1993), and tests of 'folk physics' requiring judgements to be made about the physical properties of objects (Baron-Cohen, Wheelwright, Spong, & Scahill, 1998). To date, there have been no studies examining ToM deficits in siblings of children with AS, and few concerning siblings of children with Autism. Ozonoff, Rogers, Farnham, Pennington, & Bruce, (1993) compared 18 siblings of autistic children with 18 siblings of learning disabled children on first and second order theory of mind tests. However, power analyses suggested that these measures were not sufficiently sensitive to detect the subtle differences that might exist in siblings with 'lesser variant' ToM deficits.

In summary, theory of mind deficits appear to have a unique significance in the autistic spectrum disorders, and have been conceptualised as underlying the deficits in social, communicative, and imaginative abnormalities that are diagnostic of the condition. The proposed study shall use the children's version of the "Eyes Test" (Baron-Cohen, Wheelwright, Spong, & Scahill, 1998) to examine differences between the *siblings* of index cases diagnosed with Asperger Syndrome, and a control group of normals matched on age and a

measure of verbal comprehension. The evidence from earlier studies (see above) suggests an increased incidence of various cognitive disabilities in relatives of autistic individuals. Therefore, examining theory of mind abilities in first degree relatives may suggest whether there is a familial component involved in the development of a specific neuro-cognitive mechanism, used when making judgements about the mental states of others.

The proposed study represents both a replication and an extension of the hypothesis stated by Baron-Cohen & Hammer (1997c) that parents showed a lesser variant of the 'mindreading' deficits found in their children who had Asperger Syndrome. The siblings of children affected by the clinical syndrome of Asperger Syndrome were studied because of the relative lack of co-morbidity in terms of general cognitive disability in this syndrome, and the compelling evidence regarding its heritability.

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### **3. Major Research Project Proposal**

**Mindreading difficulties in the siblings of people with  
Asperger Syndrome: Evidence for a genetic influence  
in the abnormal development of a specific cognitive  
domain.**

**\*Address for correspondence**

**Liam Dorris BSc (Hons)  
Trainee Clinical Psychologist  
University Department of Psychological Medicine  
Gartnavel Royal Hospital  
1055 Great Western Road  
Glasgow  
G12 OXH**

**1. Name and status of proposer:** Liam Dorris Bsc (Hons)  
Trainee Clinical Psychologist  
Department of Psychological Medicine  
University of Glasgow

**Supervisor:** Professor Colin Espie  
Head of Department  
Department of Psychological Medicine  
University of Glasgow

2. **Address for correspondence:** Liam Dorris  
University Dept. of Psychological Medicine  
Academic Centre  
Gartnavel Royal Hospital  
1055 Great Western Road  
Glasgow G12 OXH

**3. Employing authority:**

Greater Glasgow Community and Mental Health Services NHS Trust.

**4. In which hospital(s) or other location will the study be undertaken:**

Study to take place in participants homes, or else at convenient health service sites if more convenient.

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**5. Title of project:**

Mindreading deficits in the siblings of people with Aspergers Syndrome: Evidence for a genetic influence in the abnormal development of a specific cognitive domain.

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**6. Has the proposed research been approved by any other committee on ethics? (Give details):**

No.

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**7. Has the proposed, or similar, research been carried out in any other centre? (Give details)**

Yes, a team at Cambridge University (Baron-Cohen & Hammer, 1997a) used a similar procedure to the one intended by the present study to examine 'theory of mind' deficits in the parents' of Asperger Syndrome (AS) children. They found qualitatively similar impairments in parents of AS children, but at a lesser severity of deficit. The difference between parents of AS children and control parents was significant. This raises the possibility that a lesser variant of one of the 'core' impairments in AS and Autism may be inherited and subtly expressed by relatives who are not autistic.



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**8. Please give a summary of the project, including the question to be answered, the procedures to be used, the measurements to be made and how the data will be analysed (please see question 15 for recording details of how consent is to be obtained):**

A range of cognitive deficits has been found in autism (Ozonoff, Pennington, & Rogers, 1991), and has led to the hypothesis that cognitive deficits may underlie the social impairment. One aspect of social cognition which has been shown to be impaired in autism is the ability to fully develop a 'theory of mind', which entails being able to postulate the existence of mental states and then using them to explain and predict another person's behaviour (Baron-Cohen, 1989).

Ozonoff (1991) found that some high functioning Autistic participants were able to pass 'theory of mind' tasks. However, Baron-Cohen, Jolliffe, Mortimore, & Robertson (1997b) argued that the lack of deficits in these studies was due to the tests being too simple, being simply probes for a 6yr old level of mindreading ability. Studies in the past have suggested that around 20% of high functioning adults with Autism can pass second order theory of mind tasks (the ability to think about another person's thoughts about a third person's thoughts about an objective event). Such tests can usually be passed by normal children around the age of 6 years.

Baron-Cohen et al (1997b) used an 'adult' theory of mind test, the Eyes Test that involves inferring the mental state of a person just from the information contained in photographs of a persons' eyes. They found that all of a sample of high functioning adults with Asperger Syndrome (mean age 28yrs; mean IQ 105) showed mindreading deficits relative to age matched normals and a clinical control group (Tourette Syndrome). In a second study looking at the parents of children with AS (Baron-Cohen & Hammer 1997a), the same deficits were apparent albeit in a lesser form. Families with a child who has Asperger Syndrome show an increased rate of AS profiles amongst other relatives (e.g. Gilberg, 1991). The suggestion is that relatives of people with AS/Autism may not have the condition itself but may have a lesser variant of the disorder.

## **Research Aims**

The present study hopes to examine whether subtle deficits in mind-reading skills are apparent in the siblings of individuals with AS. If found, this would strengthen the argument that a specific cognitive deficit in 'mind-reading' has a genetic loading which is expressed amongst first degree relatives of people with AS. The following experimental hypothesis are postulated:

1. The group of siblings of people with Aspergers Syndrome shall show a worse performance on the Eyes Test, in terms of correct mental state inferences, than a matched group of normal participants.

2. These postulated deficits shall be strongest in male siblings reflecting an enhancement of the existing sex difference found in 'normals'.

### *Procedure*

Participants who have consented to take part in the study shall be asked to complete a brief measure of verbal intellectual functioning, either the National Adult Reading Test (NART), or the British Picture Vocabulary Scale version II (BPVS II), depending on age.

The second task shall be the 'Eyes Test', the version used depending on the participants age. This task requires the participant to look at photographs of the eye region of a human face, and choose which one of four mental state terms e.g. 'friendly', 'sad', 'surprised', or 'worried', best describes what the person is thinking or feeling. Total time to carry out the procedure is expected to be around 30 minutes.

### *Experimental measure:*

The experimental task is called the "Reading the mind in the Eyes test", or the "Eyes Test" for short (Baron-Cohen et al 1997b). The Eyes Test involves 'theory of mind' skills in that the subject is shown a series photographs of the eye region of the human face and invited to select one of four mental state

terms which best describes what the person is thinking or feeling. The adult version of the 'eyes test' has been shown experimentally to discriminate amongst the parent's of children with Asperger Syndrome, and parent's of non-affected children. A Child version of the test has also been developed which can be used with children over 6 years of age. The task takes around 15 minutes to complete.

### *Intelligence Assessments:*

The study requires that participant's are assessed with a measure of verbal intelligence as the Eyes Test contains a verbal component. The British Picture Vocabulary Scale, version II (*Long version*) (Dunn, Dunn, Whetton, & Burley, 1997) shall be used to assess participants aged up to 16 years. The National Adult Reading Test (NART) shall be used to assess the verbal intelligence of participants over 16 years of age.

The study uses a matched control between group design consisting of AS siblings and a group of matched 'normals'. The independent variable in this study consists of the groups themselves (i.e. AS familial +; AS familial -) and the dependent variable is score on the Eyes test. Group means shall analysed using SPSS version 7 statistical software at the Department of Psychological Medicine. One way Anovas shall be used to determine whether group variances are significantly different, and an Ancova model may be used to

adjust the means if they are found to be subject to any confounding variables such as linguistic competence.

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**9. Please state whether there are any expected benefits to patient care and, if so, summarise:**

This study is relevant to theoretical questions related to the nature, and development of mind-reading skills that are thought to fundamentally characterise the autistic individual. Findings may be useful in understanding how the transmission of a genotype may affect a familial grouping. This in turn could potentially inform studies looking for specific gene markers involved in autism.

If in the long term, measures can be developed that can detect the presence of a phenotypic 'marker' for AS/Autism, they may have utility in providing information on the possible likelihood of further offspring being affected by Autism/AS. This is a question frequently asked of Geneticists by parents of children with Autism/AS.

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**10. Please state the likely duration (a) of the project itself and (b) for individual patients:**

a) A period of around six months will be required to gather data. Collation and analysis of data, and writing up of project shall require a further three months. The project requires a completion date around Easter 1999.

b) The time required for individual subject participation shall be in the region of 30 minutes.

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**11. Please state who will have access to the data and what steps will be taken to keep data confidential:**

Professor Espie and myself shall have sole access to the data obtained during this study. All data shall be stored on a disc which shall be securely kept in a locked drawer at my home when not in transit. Analysis of the data shall be undertaken using security coded computers at the Dept. of Psychological Medicine, GRH.

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**12. Please give details of how consent is to be obtained. A copy of the proposed consent form, along with a separate patient information sheet, written in simple, non-technical language, must be attached to this proposal form.**

The support of both the National Autism Society (Glasgow), and the Scottish Society for Autistic Children has been gained, and these organisations have agreed in principal to help with the recruitment of potential participants. This would be obtained by distributing information sheets outlining the nature of the

study (which I have provided), as well as the practicalities of participating. Fiona Knott (Clinical Psychologist) has developed close links with these organisations and is currently assisting with the recruitment of participants. It is also hoped to distribute details of the study to possible participants at the Scottish Autism Centre, Royal Hospital for Sick Children, via team members there. This is of course subject to approval, and is being supported by Dr Jeff Salt (Clinical Psychologist) who is a member of the team.

Once potential participants have declared an interest in taking part, they shall be offered the chance to discuss the study at length before ultimately deciding to do so, at which point I shall ask them to read and sign the enclosed consent form.

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**13. Is the power of the study sufficient to answer the question that is being asked? Please indicate the calculations used for the required sample size, including any assumptions you may have made. (If in doubt, please obtain statistical advice).**

In order to test the predictions made above (see Research Aims above), a matched control between group design was utilised. Using data from a comparable study (Baron-Cohen & Hammer, 1997) a power calculation indicated that a sample of 25 participants per group would be adequate to test these hypotheses with 0.9 power at  $p < 0.05$  (one-tailed).

**14. What statistical tests will you apply to your results?**

**Please give details of proposed methods:**

Exploratory data analysis and matched sample t-tests shall form the initial analysis. An Analysis of Covariance (ANCOVA) model shall be used to examine the importance of variables such as sex, verbal comprehension, and age.

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**15. Scientific background to study (give a brief account of relevant research in this area with references):**

Autism is a pervasive developmental disorder that manifests in the first 36 months of life in the form of qualitative and quantitative impairments in communication, social interaction, and in restrictive, repetitive and stereotyped patterns of behaviour and interests (DSM IV, 1994). Asperger Syndrome (AS) is diagnosed in the same way but there are differences in cognitive functioning, AS individuals usually functioning in the normal range of intelligence and with better language skills than in classic autism. Both disorders are now thought to occupy a continuum with AS being nearer to normal end (Wing, 1990).

Baron-Cohen et al (1997a, 1997b) suggest that the cognitive phenotype in Autism involves a deficit in social cognition, specifically in mind-reading or 'theory of mind'. There is considerable evidence that the majority of children with Autism have impairments in the development of a theory of mind (see Baron-Cohen, 1993, 1995 for reviews). Such a deficit may underlie the social,



communicative, and imaginative abnormalities that are diagnostic of the condition, since a theory of mind is necessary for normal development in each of these three areas. Such an ability is distinct from perceptual role taking, which is intact in autism (Hobson, 1984). The theory of mind deficit appears to be expressed very early, probably from the end of the first year of life, as joint attention deficits (Baron-Cohen et al, 1996).

Asperger Syndrome is thought to be a disorder with a considerable genetic loading (Wing, 1981; Gilberg, 1991; Bailey, Le Couteur, Gottesman, Bolton, Simonoff, et al, 1995). However, there has been little attention paid to how any genetic loading may be expressed in cognitive terms, in the biological relatives of AS individuals. It has been suggested that relatives may not have the condition itself but may nevertheless have a 'lesser variant' of aspects of the condition, as a result of a genetic predisposition. The specific hypothesis that siblings of individuals with AS may show a lesser variant of the same mind-reading deficit represents an attempt to elucidate more precise cognitive phenotypes in AS/Autism.

**16. Does the research involve additional invasive procedures over and above the normal treatment of the patient? If so, are there any hazards associated with the procedure?**

Not Applicable.

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**17. Please state any other potential hazards to participants arising from the research, their estimated probability (if possible) and the precautions to be taken to meet them:**

None anticipated.

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**18. Please describe any procedures which may cause discomfort or distress to participants, the degree of discomfort or distress entailed and their estimated probability:**

It is possible that participants may feel they are being 'diagnosed' as mildly autistic should their test performance reveal difficulties in 'theory of mind' skills. To reduce the negative impact of this contingency, the study will be described as being primarily theoretical, and as having no diagnostic content. As a Psychologist with some experience of supporting people who have AS, and their families, I anticipate being able to adequately manage the majority of these concerns.

Participants who are very anxious as to their own status, or parents anxious about the status of any non-diagnosed children with autistic features shall be referred, if it is felt appropriate, to Dr Jeff Salt, at the Scottish Centre for Autism. Dr Salt has agreed to offer consultation and assessment in such circumstances.

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**19. Who are the proposed participants in the research (and controls if appropriate), and how are they to be selected? Please give details of age, sex, numbers involved and any other relevant details:**

Participants shall be:

Group 1 *Siblings* of identified person with AS (Index Cases). Siblings shall be aged 6yrs and over, and of both sexes. Index cases with a diagnosis of AS shall be gathered via the Scottish Centre for Autism, and through the Scottish Centre for Autism, and the National Autistic Society. Both of these latter organisations have agreed to help with recruitment for the study. Siblings of reliably diagnosed Index cases shall then be sent details of the study along with an invitation to take part. It is hoped to gain around 30 suitable participants.

Group 2 This group will serve as a comparison group and will consist of a similar number of 'normals', who shall be selected in terms of their matching characteristics on age, intelligence, and sex. Again, details and consent forms shall be given to control participants. The younger control participants shall be recruited from local primary schools, and I am currently in the process of contacting the Education Departments of Local Authorities to assess the best way of organising this. Older control participants shall be sought from a variety of sources including, colleagues, friends, and Undergraduate students.

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**20. Give names, strengths, doses and route of administration of investigational drugs to be used:**

Not Applicable.

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**21. Are the drugs to be used subject to the terms of:-**

**A Product Licence:**

**A Clinical Trial Certificate (CTC) or Certificate Exemption (CTS):**

**Is an unlicensed Product, but is registered under the DDX Scheme:**

**Which ever is applicable, please provide documentary evidence**

Not Applicable.

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**22. Are the drugs used being given in accordance with the Product Licence, with the agreed protocol (in the case of CTC or DDX) or with the CTC?**

**If no, give details:**

Not Applicable.

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**23. Which manufacturer is organising the trial or supplying investigational drugs?**

Not Applicable.

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**24. If the trial is being undertaken in general practice and involves the supply of drugs, please state the arrangements for storage, labelling and dispensing.**

Not Applicable.

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**25. Are questionnaires to be used? If yes, a copy must be attached to this application form.**

No.

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**26. How is the project to be funded?**

D.Clin.Psych programme expenses allowance.

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**27. Please state any 'interests' i.e. profit, personal or departmental, financial or otherwise, relating to the study. Details of payments per patient recruited, and/or any other remuneration details must be included.**

Study has personal 'interest' insofar that it forms part of the requirements for my Doctoral degree, which forms my professional qualification as a Clinical Psychologist.

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**The information supplied above is to the best of my knowledge and belief accurate. I have read the notes to investigators and clearly understand my obligations and the rights of the subject, particularly in so far as to obtaining freely given informed consent. I also confirm that I have read and understood "*The Declaration of Helsinki*"**

**Date of Submission:**

**Signature of Principal Investigator:**

## References

- 1 Baron-Cohen & Hammer (1997a) "Parents of Children with Asperger Syndrome: What is the Cognitive Phenotype" *Journal of Cognitive Neuroscience*, 9:4, pp548-554.
- 2 Ozonoff , Pennington, & Rogers (1991 "Executive function deficits in high functioning autistic children: Relationship to Theory of Mind." *Journal of Child Psychology and Psychiatry*, 32, 1081-1106.
- 3 Baron-Cohen (1989) "The autistics childs' theory of mind: A case of specific developmental delay". *Journal of Child Psychology and Psychiatry*, 30, 285-298.
- 4 Baron-Cohen, Jolliffe, Mortimore, & Robertson (1997b) "Another Advanced Test of Theory of Mind: Evidence from Very High Functioning Adults with Autism or Asperger Syndrome", *Journal of Child Psychology and Psychiatry*, vol 38, no 7, pp813-822.
- 5 Gilberg (1991) "Clinical and neurobiological aspects of Asperger syndrome in six family studies. In U. Frith (Ed), *Autism and Aspergers' syndrome*. Cambridge, Eng.: Cambridge University Press.
- 6 Dunn, Dunn, Whetton, & Burley, (1997) *The British Picture Vocabulary Scale*,  
*version-II*. NFER-NELSON.

**7** American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition. Washington, DC, American Psychiatric Association, 1994.

**8** Wing, L. (1990) "The continuum of autistic characteristics". In E Schopler & G. Mesibov (Eds), *Diagnosis and assessment in autism*, (ch.7). New York: Plenum.

**9** Baron-Cohen, Tager-Flusberg, & Cohen (Eds.) (1993) "Understanding other minds: Perspectives on Autism." Oxford, Eng.: Oxford University Press.

**10** Baron-Cohen (1995) "Mindblindness: An essay on Autism and Theory of Mind". Cambridge, MA: MIT press/Bradford Books.

**11** Hobson, R.P. (1984) "Early childhood Autism and the question of egocentrism". *Journal of Autism and Developmental Disorders*, 14, 85-104.

**12** Baron-Cohen, Cox, Baird, Swettenham, Drew, Nightingale, Morgan, & Charman (1996) "Psychological markers of Autism at eighteen months of age in a large population." *British Journal of Psychiatry*, 168, 158-163.

**13** Wing, L. (1981) "Asperger's Syndrome: a clinical account" *Psychological Medicine*, 11, 115-129.



**14** Bailey, A., Le Couteur, A., Gottesman, I., Bolton, P., Simonoff, E., Yuzda, E. (1995) "Autism as a strongly genetic disorder: evidence from a British twin study" *Psychological medicine*, 25, 63-77.

#### **4. Major Research Paper**

**Mind-reading difficulties in the siblings of people with Aspergers Syndrome: Evidence for a genetic influence in the abnormal development of a specific cognitive domain.**

**Liam Dorris BSc (Hons)**

**31<sup>st</sup> July 1999**

**Major Project submitted in fulfilment of the requirements for the degree of Doctor of Clinical Psychology.**

**Prepared in accordance with the guidelines for contributors to the 'Journal of Child Psychology and Psychiatry'.**

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G12 0XH**

## **Abstract**

**Introduction:** Previous research suggests that the phenotype associated with Asperger Syndrome (AS) includes difficulties in understanding the mental states of others, leading to difficulties in social communication and social relationships. It has also been suggested that the first-degree relatives of those with AS can demonstrate similar difficulties, albeit to a lesser extent. This study examined 'theory of mind' (ToM) abilities in the siblings of children with AS relative to a matched control group. **Method:** 27 children who had a sibling with AS were administered the children's version of the 'Eyes Test' (Baron-Cohen, Wheelwright, Spong, & Scahill, 1998). The control group consisted of 27 children matched for age, sex, and a measure of verbal comprehension, and who did not have a family history of AS/Autism. **Results:** A significant difference was found between the groups on the Eyes Test, the 'siblings' group showing a poorer performance on this measure of social cognition. The difference was found to be more pronounced amongst female siblings. **Discussion:** These results are discussed in terms of the familial distribution of a neuro-cognitive profile associated with AS, which confers varying degrees of social handicap amongst first-degree relatives. The implication of this finding with regard to the Autism/AS phenotype is explored, with some discussion of why this neuro-cognitive profile (in combination with corresponding strengths) may have an evolutionary imperative.

**Keywords:** Asperger Syndrome, mind-reading, lesser variant deficits in siblings.

## **Introduction**

Autism and Asperger syndrome are pervasive disorders of development characterised by abnormal difficulties in social relationships, communication, and imagination (DSM IV, American Psychiatric Association, 1994; ICD-10, World Health Organisation, 1993). These classification systems suggest that a diagnosis of Asperger Syndrome applies when there is no clinically significant delay in language development, and intelligence is in the normal range (Prior, Eisenmajer, Leekam, Wing, Gould, et al, 1998).

Since autism was first described by Kanner (1943) researchers have been speculating about the role of genetic factors in the aetiology of autism. Folstein & Rutter (1977) suggested a genetic hypothesis, conceptualising a continuum of underlying genetic risk for autism, with the full syndrome as the most severe phenotype. These authors suggest that it is not autism as such that is inherited, but rather a pervasive cognitive deficit of which autism is one part. Twin studies offer strong support for the genetic contribution to autism by indicating a greater MZ than DZ concordance for autism and autistic spectrum disorders (Folstein & Rutter, 1977; LeCouter, Bailey, Rutter, & Gottesman, 1989). For example, Bailey, LeCouter, Gottesman, Bolton, Simonoff et al (1995) combined their data with that from earlier studies and found an MZ concordance rate of 60%, and a DZ rate of 0%. The minimum prevalence of AS has been stated as 3.6 per 1000 children, with a male to female ratio of 4:1 (Ehlers & Gillberg, 1993).

Delineating specific behavioural or cognitive phenotypes has the potential to isolate more specific subgroups within the autistic spectrum. A range of cognitive deficits has been found in autism (Ozonoff, Pennington, and Rogers, 1991), and has led to the hypothesis that cognitive deficits may underlie the social impairment. One aspect of social cognition which has been shown to be impaired in autism is the ability to fully develop a 'theory of mind', which entails being able to postulate the existence of mental states and then using them to explain and predict another person's behaviour (Baron-Cohen, 1989). The 'theory of mind' deficit account of autism suggests that the communication, socialisation and imagination handicaps of autistic individuals spring from their inability to represent and attribute mental states (Frith, 1989; Leslie, 1987, 1988). Strong claims have been made over the past decade for the centrality of this ability, or rather disability, in the social/cognitive profiles of autistic children. Indeed it is claimed that it is this "mind blindness" that is the core of the disorder (See Baron-Cohen, 1989; Frith, 1989; Happe, 1994).

Given the evidence that Autism/AS have a strong heritability factor (see above), it might be fair to assume that aspects of the phenotype such as difficulties in social relationships might be evident amongst family groups. Recently, Baron-Cohen et al (1998) have suggested that if a brain has a genetically-based impairment in 'folk psychology' (our everyday understanding of people in terms of mental states), or a genetically-based talent for 'folk physics' (our everyday understanding of objects in terms of physical causality and spatial relations), this could lead the individual (brain) to spend less time interacting with the social environment, and more time interacting with the physical environment.

A series of experiments has provided evidence that such a profile is indeed characteristic of individuals with AS, and that lesser variants of these information processing biases are observable in first degree relatives (Baron-Cohen & Hammer, 1997a; 1997b; Halpern, 1992). It has been suggested that AS/Autism represent the 'amplification' of the normal male brain state as defined by various psychometric tests. Baron-Cohen & Hammer (1997a) report a series of experiments looking at normal sex differences on tasks of social cognition and spatial abilities, and also at children with AS or high-functioning Autism (HFA) and a group of parents of children with AS. These experiments are reported below, the reported differences were statistically significant.

- 1) Normal males (mean speed=46.2secs, sd=20.5) were superior to normal females (mean speed=66.7, sd=36.7) on the *Embedded Figures Test (EFT)*.
- 2) Normal females (mean score=21.8, sd=1.8) were superior to normal males (mean score=18.8, sd=2.5) on the *Eyes Test* (see below for description of this test).
- 3) Nine year old girls were superior to nine year old boys on the '*Faux Pas*' Test (identifying which of three characters "said something they shouldn't have" in a story), girls mean score=7.3 (sd=2); boys mean score= 4.9 (sd=2.7).
- 4) Adults with AS/HFA were superior to age matched normals on the *EFT*, mean speed in seconds= 29.28 (sd=21.6) for the HFA subjects, versus mean

speed=32.2 (sd=27) in the AS group; versus mean speed=52.6 (sd=32.6) in the controls. The difference between AS/HFA versus normals was statistically significant.

- 5) Adults with AS/HFA were impaired relative to age-IQ matched normal controls on the *Eyes Test*, mean score=16.3 (sd=2.9), versus control mean score of 20.3, (sd=2.63).
- 6) Children with AS/Autism were impaired on the '*Faux Pas*' test relative to normal age-mental age matched controls, the AS/Autism children had a mean MA of 13 years but their mean score was equivalent to that of normal 7 to 8 year olds.
- 7) Mothers of children with AS were significantly faster than 'normal' mothers on the *EFT*, mean=48.6, (sd=31.8); versus mean=66.7, (sd=36.7), as were AS fathers, mean score= 32.8, (sd=17.7) compared to male controls, mean score=46.2, (sd=20.5).
- 8) Parent's of AS children were impaired on the *Eyes Test* relative to normal controls, AS mothers mean score=18.9, (sd=2.1) versus control mean score=22.1, (sd=2); and AS fathers mean score=17.3, (sd=1.6) versus control mean=19.5, (sd=2.6).

They conclude from these experiments that outcomes reflect the existence of sex-linked neurodevelopmental processes in the population, and that AS/Autism

is an extreme form of the male neurodevelopmental pattern. This model defines the *male brain type* as an individual whose folk physics skills are in advance of his or her folk psychology skills, regardless of biological, chromosomal sex. (The *female brain type* is posited to reflect the opposite preference). A third interaction allows for equal preference and probably encompasses the majority of individuals (in keeping with models of the normal distribution). Hence, there is huge variation in the distribution of these cognitive styles both within and between the sexes. The mechanism/s through which the AS/Autism phenotype might appear are unclear, but might include having two parents, both of whom have the brain type associated more with male sex.

In summary, theory of mind deficits appear to have a unique significance in the autistic spectrum disorders, and have been conceptualised as underlying the deficits in social, communicative, and imaginative abnormalities that are diagnostic of the condition.

The proposed study shall use the children's version of the "Eyes Test" (Baron-Cohen et al, 1998) to examine differences between the *siblings* of index cases diagnosed with AS, and a control group of normals matched on age and a measure of verbal comprehension. Examining theory of mind abilities in first degree relatives may suggest whether there is a genetic/familial component involved in the development of a specific neuro-cognitive mechanism used when making mentalistic judgements. The proposed study represents both a replication and an extension of the findings of Baron-Cohen & Hammer (1997b), that parents showed a lesser variant of the 'mindreading' deficits found in their



children who had AS. The relatives of those suffering from the clinical syndrome of AS were studied because of the relative lack of co-morbidity in terms of general cognitive disability in this syndrome, and the compelling evidence regarding its heritability.

## **Methods**

### **Experimental Design**

The following hypotheses underpinned the study:

- 1) Siblings of children with AS will demonstrate poorer performance on the Eyes Test than a group of non-affected children matched on age and a measure of verbal comprehension.
- 2) There will be sex differences both between and within groups, with males demonstrating lower scores than females.

In order to test these predictions a matched control between group design was utilised. Using data from a comparable study (Baron-Cohen & Hammer, 1997b) a power calculation indicated that a sample of 25 participants per group would be adequate to test these hypotheses with 0.9 power at  $p < 0.05$  (one-tailed).

### **Participants**

Two groups of participants were tested:

The 'Siblings' group comprised 27 children all of whom had a sibling with a clear diagnosis of Asperger Syndrome (AS), defined according to internationally

recognised criteria as stated in the International Classification of Diseases-10, (1994). The majority of the index cases (i.e. the children with the diagnosis of AS) were diagnosed within the Scottish Centre for Autism, at the Royal Hospital for Sick Children, Glasgow. The SCA is a specialist resource providing both assessment and treatment for children suffering from a range of communication disorders. Experienced Child Psychiatrists within the context of a Child Development Clinics diagnosed the remainder. Participants were recruited via the SCA, and also via local support groups in Strathclyde and Fife. The siblings of these children were then selected on the basis of their being aged over six years. The children's version of the Eyes Test has yet to be published, but the test author (Baron-Cohen, personal communication) advised that children could use the test from about age six onwards.

There was no upper age limit as the adult version of the Eyes Test was also made available. The children comprised 18 males and 9 females, and age ranged from 7yrs 6mths to 17yrs, with a mean of 11 yrs. All participants were assessed using the British Picture Vocabulary Scale, version II (*Long version*) (Dunn, Dunn, Whetton, & Burley, 1997). Their BPVS II scores ranged from 7yrs 3mths-17yrs, (mean score= 11yrs 6 mths). Table 1 shows the mean age, and mean score on the BPVS-II, along with standard deviations for both experimental groups.

The 'Control' group comprised 27 children attending primary and secondary schools in Ayrshire, West Lothian, and Fife. Letters explaining the study were distributed widely in these schools and participants were selected from a larger

number of responders on the basis of their matching characteristics to the siblings group in terms of sex, age, and score on the BPVS II. The matching was conducted primarily on the basis of age and sex for practical reasons, although large differences in BPVS-II scores led to de-selection where an alternative participant was available. Selection criteria included being aged over six years and critically, not having a family history of Autism/AS. None had been given a record of needs as having any special educational requirements. The ages of this group ranged from 7yrs 4mths to 17yrs 7mths, with a mean age of 11 yrs 8mths. Their BPVS II scores ranged from 7 years 1mth to 17yrs, (mean=11yrs 8mths). Ethical approval was obtained to conduct this study from three NHS Trusts including Greater Glasgow Primary Care NHS Trust, Yorkhill Hospitals NHS Trust, and Ayrshire & Arran NHS Trust.

### Procedure

All participants were given two tests:

Firstly, the children's version of the 'Eyes Test' was administered (Baron-Cohen et al, 1998). Examples of this test are shown in Appendix 4.0. The test consists of 28 photographs of the eye region of the human face, and the participant is asked to choose one word from a list of four which best describes what the person is thinking or feeling. The test was administered in the participant's own home, or else in their school, and typically required around 15 minutes to administer. Adapted from the Adult version of the Eyes Test (Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997c), the main change concerns the

reduction in linguistic complexity of the target and foil words. The test was piloted with a sizeable number of children ( $n=53$ ) and only those items which were reliably and correctly selected (i.e. selected by  $>50\%$  of children) were retained (see unpublished manuscript by Baron-Cohen, Wheelwright, Spong & Scahill for full details of test construction).

Secondly, all participants were administered the BPVS-II. This frequently used test is a measure of receptive vocabulary, which is an important indicator of verbal intellectual competence. This was used to derive a measure of verbal comprehension, which was transformed into a standardised age normative score. The test requires around 20 minutes to administer, bringing the total time to administer the protocol to around 40 minutes.

## **Results**

Summary results showing scores on the Eyes Test, the British Picture Vocabulary Scale II (BPVS-II), and Age are shown for both groups in Table 1. The participants were sex matched, and matched as closely as possible for both Age and score on the BPVS II. The difference between groups was non-significant for both these latter variables ( $p > 0.05$ ). In order to investigate the predicted group difference on the Eyes Test a related-samples *t*-test was used. The Siblings group performance on the Eyes Test was significantly worse than the group of Age/BPVS-II matched controls [ $t = 1.968$ ,  $df = 26$ ,  $p = .030$ ].

Figure 1 offers a visual inspection of differences between matched pairs on the Eyes Test. From a total of twenty-seven pairs, control participants scored higher than siblings in 16 (59.3%) cases, whilst no difference was found in 3 (11.1%) cases. However, in 8 (29.6 %) cases the sibling achieved a higher score on the test than the matching control participant. It can also be seen from Figure 1 that siblings cases 9, 11, 12, 19, & 22 scored over 20 on the Eyes Test, or put another way, identified the correct mental state term on over 70 % of test items. Overall, the majority of siblings (almost two-thirds) showed a poorer performance on the Eyes Test than their matched controls. The opposite disparity in performance was found in almost one-third of cases, where the siblings often showed a relatively high level of performance on this test of social cognition.

*Insert Table 1 Here*

*Insert Figure 1 Here*

In order to assess whether any other factors might account for this difference, the relative importance of sex, BPVS-II score, and age were analysed separately. Score on the BPVS-II was found to be significantly correlated with score on the Eyes Test [ $r = .414$ ,  $p = .003$ ], as was Age [ $r = .346$ ,  $p = 0.01$ ], using Pearsons' product-moment correlation coefficient analyses. There was also a significant gender effect across the total sample [ $n = 54$ ,  $t = -3.967$ ,  $df = 52$ ,  $p = .0001$ ] with females outperforming males. Independent sample t-tests were also used to examine this sex difference between groups and showed that control females scored significantly higher on the Eyes Test than female siblings ( $p = 0.022$ , two-tailed), replicating the results of Baron-Cohen & Hammers' 1997 study of parents of children with AS. Control males also scored higher than male siblings, although this difference was not found to be significant ( $p > 0.05$ ). Figure 2 shows mean scores on the Eyes Test as a function of group and sex.

*Figure 2 Here*

In order to take into account the contribution of these factors in explaining the overall group difference, a factorial ANCOVA model was used. The independent variables included Sex (male, female) and Group (sibs, controls), with Age and BPVS-II score entered as covariates. The results of this analysis are presented in Table 2. Inspection of Table 2 reveals that age and verbal comprehension (combined) were indeed significant influences upon the Eyes Test scores ( $p = .016$ ). However, when removed from the equation by means of the ANCOVA analysis, main effects for both group and gender remained. In other words control participants outperformed siblings of people with AS, and females outperformed males ( $p = .0225$ ;  $p < .0001$ ; respectively). These were independent effects since the interaction term (group $\times$ sex) was found not to be significant.

***Insert Table 2 Here***

In order to consider the possibility that differential performance effects might relate to a developmental pattern, mean test scores were plotted along six different age bands consisting of two-year intervals (Figure 3). A one-way ANOVA showed a non-significant difference on Eyes Test scores in terms of age-group in the siblings group [ $F(5,1) = .199$ ,  $P = .959$ ], but did find a significant



scoring significantly lower than the other groups [ $F(5,1) = 3.84, P = .013$ ]. Figure 3 shows the distribution of scores across the age bands for both siblings and controls. As can be seen, there is a plateau in the sibling's performance at around the 8-10 year-old level, with a slight regression amongst 14-17 year-old levels. The controls show a fairly consistent improvement over time with notable improvements at the 10-12 year level, and again at the 14-16 year level. These conclusions are tempered by the small numbers involved in these distributions, but represent phenomena worthy of future study involving much larger sample sizes.

***Figure 3 Here***

## **Discussion**

The main predictions of this study were confirmed, namely that: i) siblings of AS children were significantly poorer on the Eyes Test, a test of social cognition, than a group of matched controls; and ii) males were significantly poorer on the test than females, both within and between groups. This study provides further evidence for the conclusion, as suggested by others (Piven, Wzorek, Landa, Lainhart, Bolton et al, 1994; Piven & Palmer, 1997; Hughes, Plumet, & Leboyer, 1999; Baron-Cohen et al, 1998), that first degree relatives of AS children are affected by a milder variant of the neuro-cognitive profile associated with AS/Autism. In this case the profile involves modest but statistically significant deficits in mental state awareness, or 'theory of mind' skills.

Hypothesising the relationship of a proposed phenotype to an underlying gene structure is beyond the scope of research such as the present study. However, specifying exactly what is meant by the 'broader phenotype' of AS/Autism is a source of debate. LeCouter, Bailey, Goode, Pickles, Robertson et al (1996) define the broader phenotype as the presence of clinically significant communication impairment or social dysfunction either alone or in combination. Of the present sample of AS siblings, few were noticeably affected by pervasive difficulties in social communication, and the majority would probably not be considered as showing the 'broader phenotype' as defined by LeCouter et al, (1996). However, increasing the specificity with which cognitive profiles are investigated can indicate the presence of difference/deficit in the absence of

even sub-clinically significant impairment in social and/or communicative spheres in relatives of AS/Autistic individuals.

Any theory outlining the cognitive '*phenotype*' of AS/Autism must accept that genes can influence behaviour relatively directly, as phenotype implies genotype. In the case of mental state awareness or 'theory of mind', it would appear that the genotype does exert an influence throughout the familial grouping. However, the phenotypic expression of this influence is variable and probably multi-determined, involving normal variation of a genetically influenced trait/s rather than the direct influence of an abnormal gene. Baron-Cohen et al, (1998) suggest that there is a preference for non-social learning environments in AS, and that this preference results in the development of expertise in areas such as mathematics, engineering, and activities requiring knowledge of physical causation and logical relationships within the physical world. This gene-environment interaction presumably also exerts an influence in AS relatives, but to a lesser extent; and whilst individuals may develop expertise in social and/or non-social learning environments, they may always subtly evidence the genetic liability in theory of mind skills, such as those found by the Eyes Test.

To date, there have been no published studies examining social learning accounts of theory of mind development in children who have an AS sibling and/or other family members with AS traits. However, studies of normally developing children suggest that the presence of older siblings facilitates false belief understanding in children aged 3-4 years (e.g. Ruffman, Perner, Naito,

Parkin, & Clements, 1998). It has also been suggested that the number of adults and/or older children interacted with daily, can also have a positive influence on tests of false belief (Lewis, Freeman, Norman, Kryiakidou, Maridaki-Kassotaki, et al, 1996). A further study by Jenkins, Astington, & Wilde (1996) found that false belief test scores were higher in children from larger families even after the effects of age and linguistic ability had been partialled out. They also found that this effect was strongest in those children who were less competent linguistically, suggesting that the presence of siblings can compensate for slower language development in developing false belief understanding. It seems that the apprentice 'theory of mind' student is influenced by interaction with a number of people within their environment, but that the availability of elder siblings may be an important factor in the development of ToM abilities. The present study gathered data on number of siblings in the siblings group, and although the sample size is relatively small, it may be combined with future samples in order to examine the important issue of social learning in siblings of children with AS.

What might be a practical implication of such a phenotype? A finding mentioned previously in the literature concerns the occupation of the parents of children with AS. Baron-Cohen et al (1997) in a family study (n=1000) found that fathers and grandfathers (patri- and matrilineal) of children with AS/Autism were more than twice as likely to work in the fields of engineering, compared to control groups. Amongst the present sample of families around half of the fathers were engineers, or else worked in related fields. Hans Asperger (1944)

himself wrote of the social value of this trait, "Many of the fathers of our autistic children occupy high positions, despite their notable peculiarities. This testifies to the social value of this personality type", (cited Frith, 1991; p84).

Related to this, many of the parents of the present sample reported that their non-AS children had a discrepancy in their abilities at school, often preferring maths and science subjects. Peer-relationship problems were also reported relatively frequently, although this information was not recorded. Although this anecdotal evidence has little stand-alone worth, it is interesting when combined with the definite incidence rates of career preference in male relatives of AS individuals.

Although most people with AS/Autism are male (Wing, 1981, suggests a m/f ratio of 9:1), the present study found that female siblings showed a greater deficit relative to female matched controls. This is in keeping with the idea, as posited by Baron-Cohen et al (1998), that they display a greater familial loading for the *male brain state*, and although they retain their superiority over male controls they show a relatively greater deficit compared to control females. Perhaps then, female AS sufferers require a greater genetic loading than males in order to attract a diagnosis. This would be in keeping with anecdotal reports of female AS sufferers being more severely affected by the condition. Clearly, further research is required to address this question, and may require a reconsideration of the diagnostic threshold of AS in females.

A methodological issue arising from the present study concerns the 'purity' of the Eyes Test as a measure of theory of mind ability. For example, might the linguistic content of the test contribute variance into the measure, confounding observation of 'pure' ToM processes. Presently, the neural substrate/s underlying theory of mind abilities is unknown. There is debate regarding whether 'theory of mind' has a modular basis within the brain (see Baron-Cohen, 1995), or whether it is evoked through the activation of a distributed set of neural networks (see Goel, Grafman, Sadato, & Hallet, 1995). Evidence from brain-imaging studies, and studies of patients with known brain pathology, implicate several such circuits as being involved in ToM tasks (e.g. Baron-Cohen, Ring, Moriarty, Schmitz, Costa et al, 1994; Stone, Baron-Cohen, & Knight, 1998). For example, Brothers & Ring (1992) suggest that the amygdala and the orbito-frontal cortex are involved in what they describe as the 'hot' aspects of ToM, that is, for interpreting the valence and significance of other's actions and intentions.

It is, therefore, likely that the psychological construct of 'theory of mind' does not correspond to a unitary module within the brain, but exists as a collection of inferential abilities drawing upon both sensory and linguistic, and other cognitive processes. In keeping with this theory, Stone et al (1998) propose that to make an inference about what another person may be thinking, many areas of the brain must be working together. Therefore, deciding what constitutes a 'pure' theory of mind task is a methodological problem informed by hypothetical assumptions of what ToM consists of.

Future research may further explore these neuro-cognitive profiles by studying their pervasiveness throughout wider familial groupings. This would require the use of increasingly sophisticated psychometric techniques, in order to discriminate sub-clinical cognitive markers. An improvement on the current test, the Eyes Test, might be to incorporate a response time latency measure. This would provide data regarding the 'effortfulness' as well as accuracy of mental state inferential judgements. The influence of social learning models in familial groups affected by the AS phenotype also requires rigorous investigation. The double handicap of having a genetically based predisposition towards having some difficulty with social cognition, and having family members whose social interactions may be less than optimal, may leave many AS siblings vulnerable to developing difficulties in social communication. Perhaps this kind of research may lead to early intervention approaches in such families in order to maximise development in these key areas.

In summary, it has been proposed that the wide ranging deficits seen in autistic disorders result from a few primary cognitive deficits (Baron-Cohen, 1995; Hughes et al, 1999; Frith, 1989). It is further proposed that the difficulties in mental-state awareness cause the deficits in sociability and communication that are the hallmark of AS/Autism (e.g. Baron-Cohen, 1995). This study has shown a lesser variant of the same theory of mind deficit in the siblings of children with AS, providing further evidence for the validity of this cognitive profile as being a central feature of the phenotype expressed by individuals with AS.

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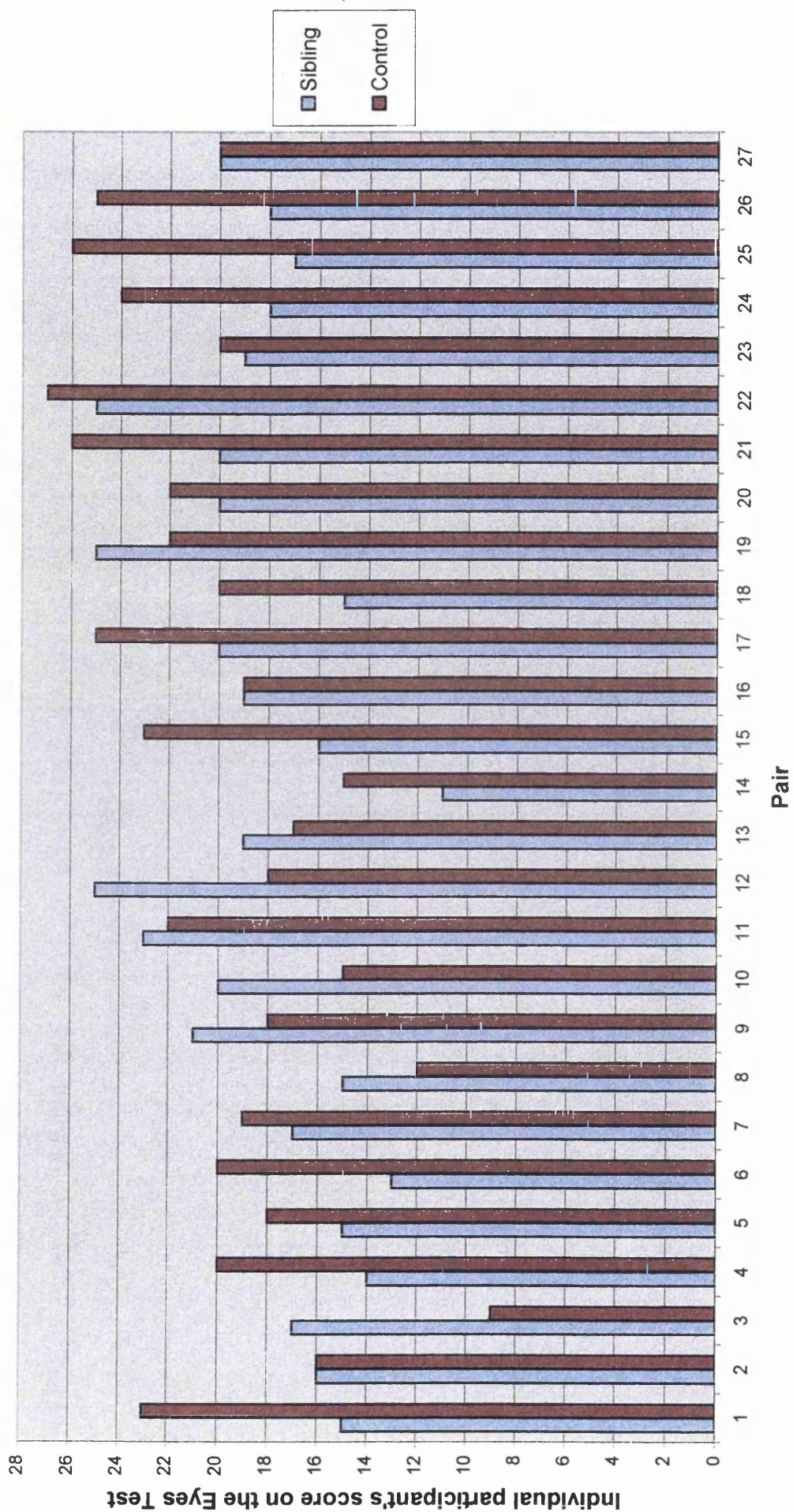
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**Table 1. Summary results showing mean scores on the Eyes Test, mean BPVS-II scores, and mean age, for both experimental groups (siblings and controls).**

	<b>N</b>	<b>Eyes Test</b> Mean (sd)	<b>AGE (Months)</b> Mean (sd)	<b>BPVS-II (Months)</b> Mean (sd)
<b>Siblings</b>	27	18.26 (3.61)	132.70 (34.10)	138.64 (34.18)
<b>Control</b>	27	20.04 (4.35)	132.48 (35.41)	139.76 (33.92)

### **Figure Legend**

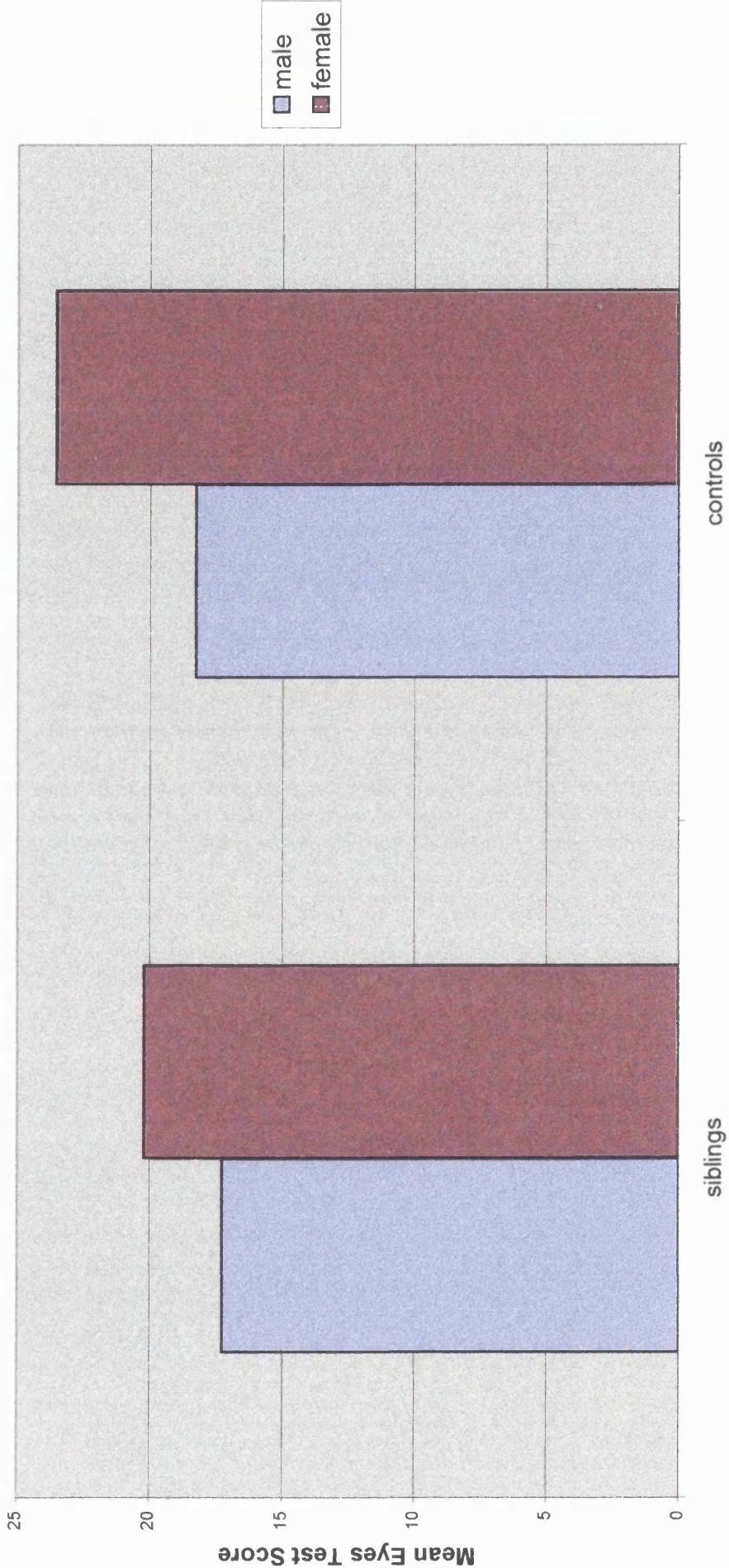
**Figure 1. Visual inspection of difference in Eyes Test scores between individual paired samples (n=27 pairs), matched on age and a measure of verbal comprehension. This figure shows that siblings scored more poorly than their matching control participant in sixteen (59.3%) cases, whilst scoring higher than matched controls in eight (29.6%) cases.**





### **Figure Legend**

**Figure 2. Performance on the Eyes Test as a function of Group (Siblings vs Controls), and sex. Differences in mean scores show that female sex predicts enhanced test performance regardless of group, with female siblings outperforming male controls. It can also be seen that the discrepancy in performance between female siblings and female controls is greater than that found in the males.**

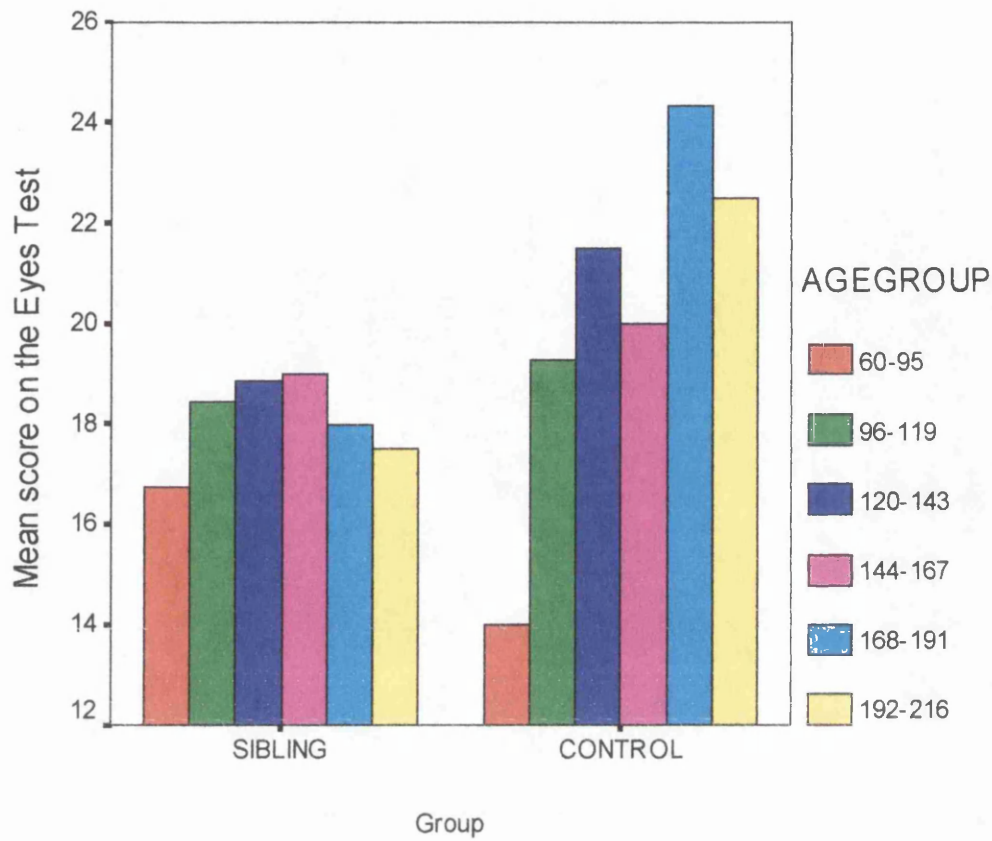


**Table 2. Results of factorial ANCOVA analysis examining differences between Siblings and Controls with both Age and score on the BPVS-II as covariates.**

			df	Mean Square	F	Sig.
<b>Eyes Test</b>	Covariates	(combined)	2	49.981	4.575	<b>.016</b>
		BPVS-II	1	6.945	.676	.415
		AGE	1	10.623	1.035	.315
	Main effects	(combined)	2	102.085	9.942	<b>&lt;.0001</b>
		GROUP	1	43.702	4.256	<b>.0225</b>
		SEX	1	160.412	15.622	<b>&lt;.0001</b>
	2-way interactions		1	26.707	2.601	.114
GROUP*SEX						

## Figure Legend

**Figure 3. The distribution of mean scores on the Eyes Test as a function of age-group (months), and of group (siblings vs Controls). The distribution of scores in the Siblings group suggest a plateau in test performance occurring at around the 10-12 year-old level, with mean scores remaining below 20 on the Eyes Test. The distribution in the Controls shows a relatively sustained improvement in test performance with increasing age. The mean Eyes Test scores in the controls stay above 20 after an age level of around 10-years.**



## **5. Clinical Case Research Study 1 (Abstract)**

# **Chronic Fatigue Syndrome: Do we need to alter physical illness attributions?**

**Prepared in accordance with the notes for contributors to the journal  
'Behaviour and Cognitive Psychotherapy'.**

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## **Abstract**

Chronic fatigue syndrome (CFS) is a disorder defined by consensus criteria, characterised by severe and prolonged fatigue, which affects physical and mental functioning, and for which no medical cause can be found (Wearden & Appleby, 1996). The cognitive-behavioural treatment model, in which the interaction of behaviour and beliefs is critical, has been developed for patients with CFS. Several studies have suggested that physical illness attributions are associated with poor prognosis in CFS.

The present case describes the treatment of a 47-year-old male, diagnosed with CFS after failing to recover from a suspected case of Legionnaire's disease. The patient was difficult to engage and maintain in therapy, held rigid views regarding his illness as having a viral cause, and resisted consideration of psychological factors relevant to his condition. Although the patient's level of somatic symptomatology remained high, clinically significant improvements in mood and adaptive behaviour were reported. This case study supports the findings of a previous study (Deale, Chalder, & Wessely, 1998) that causal attributions are less important than beliefs and behaviours related to avoidance in perpetuating CFS.

## **6. Clinical Case Research Study 2 (Abstract)**

### **The management of Tourette's Disorder in a 10-year-old boy: Involving the family in treatment.**

**Written in accordance with the notes for contributors to the journal  
'Child Psychology and Psychiatry'.**

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## **Abstract**

The case is described of a 10-year-old boy who presented with motor and vocal tics, obsessive-compulsive behaviours, and several specific anxieties related to his physical appearance and performance at school. His symptom profile was consistent with a diagnosis of Tourette's Disorder (TD) (DSM IV; 307.23).

Assessment revealed a similar history in the father, who continued to manifest residual symptoms. The patient's mother was being treated for depression, and it was felt that M's condition was being used as a focus for his parents to express negative affect towards each other. The variability of M's symptoms and their relationship with fluctuations in family systems are discussed with particular regard to the interventions used. The results of the case study suggest that the management of TD may, in some cases, be assisted through the participation of family members in a psycho-educational approach addressing emotional and familial factors, as well as direct treatment of the symptoms of the disorder.

## **7. Clinical Case Research Study 3 (Abstract)**

# **The Neuropsychological Assessment of an 8-year-old boy with a suspected case of Paediatric Autoimmune Neuropsychiatric Disorders associated with Streptococcus (PANDAS).**

**Prepared in accordance with the notes for contributors to 'Clinical Child Psychology and Psychiatry'.**

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**Abstract**

The case is reported of an eight-year-old boy who presented with abnormal movements and chorea, optic neuritis, and fever. He was admitted to hospital and treated medically. He was subsequently diagnosed with Paediatric Autosomal Disorders associated with Streptococcus, a childhood neurobehavioural disorder that arises by post-infectious autoimmune mechanisms. Neuropsychological assessment was undertaken in order to assess the functional effects of this disorder and to monitor the development of any secondary behavioural disabilities. Upon investigation, it became clear that some of the deficits within his psychometric profile were attributable to the effects of post-traumatic symptoms, suffered as a consequence of a single traumatic event, occurring in the context of a sudden, serious illness. The differentiation of these conditions allowed the effective treatment of the concurrent psychological morbidity in this patient.